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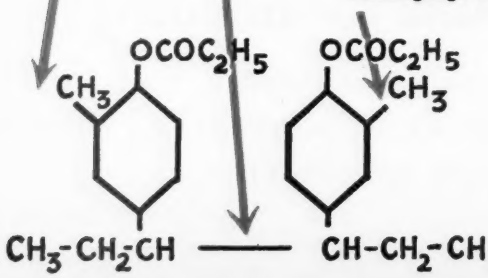

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American Journal of Obstetrics and Gynecology

VOL. 57 JANUARY, 1949 NO. 1

American Gynecological Society

Transactions of the Seventy-First Annual Meeting, May 24 to 26, 1948, at Williamsburg, Virginia

ADDRESS OF THE PRESIDENT*

EMIL NOVAK, M.D., BALTIMORE, MD.

TO BE elected a Fellow of this Society is a great distinction, and one which can be attained by only a small fraction of the gynecologists and obstetricians of our own country and its good neighbor country to the north. To be elected its President is the highest honor which can come to any of us, and the deep appreciation, mingled with a sense of deep humility, which I myself feel must be the common reaction of every recipient of this honor. However I may feel about my inadequacy to fill a post once occupied by such men as J. Marion Sims and Thomas Addis Emmett, there is one point on which I yield to no one, and that is in my devotion to this Society and what it represents, as the emblem society of our specialty. Around it revolve the most pleasant associations of my own professional life.

As I mentioned in the few incoherent remarks of appreciation which I made at our last meeting, when still dizzy from my sudden and unexpected elevation to this pinnacle, there is no man in this Society whom I dislike, many whom I like very much, and not an inconsiderable group for whom I feel a deep affection.

Our last meeting was a most enjoyable and successful one, but it was marred by the fact that my distinguished predecessor in this office, Dr. Norris W. Vaux, was stricken with a serious illness shortly before the meeting. Both he and we were thus deprived of the privilege of having him occupy the presidential chair to which he had so deservedly been elevated, and which he would have filled with the efficiency, dignity, and charm so characteristic of him. We rejoice

*Presented at the Seventy-First Annual Meeting of the American Gynecological Society, Williamsburg, Virginia, May 25, 1948.

NOTE: The Editors accept no responsibility for views and statements of authors as published in their "Original Communications."

that his health has been so much improved that he is with us again on this occasion, and I know how sincerely every Fellow of this Society hopes that he will grace our gatherings for many years to come.

During the past year, the shoulder tap of death has called from our rank three of our oldest and most respected Active Fellows: Drs. James R. Goodall, Curtis F. Burnam, and Henricus J. Stander. This is not the place to set forth their contributions to our Society or to our specialty, and this will be more appropriately done elsewhere in our Transactions. Suffice it here to say that their loss is deeply mourned by all of us, and that it leaves a painful gap in our ranks.

Equally heavy have been the losses among our Honorary Fellows since our last meeting, the list including two of our six American Honorary Fellows and one of the foreign group. Dr. Robert Meyer, whose epoch-making scientific contributions are known to all of you, died on Dec. 12, 1947. It was my privilege, at our meeting in Hershey two years ago, to present a biographical review of his life and works. Now that he has passed on, I am happy to think that some record of his career, however inadequate, is permanently inscribed in our archives.

Dr. Frank F. Simpson, who died on Feb. 10, 1948, played an active part in the life of our Society before his retirement many years ago, and was its president in 1917. He was secretary-general of the Seventh International Congress of Obstetricians and Gynecologists in 1912. Finally, the most newly-elected of our Foreign Honorary Fellows, Dr. Louis Carnac Rivett, the Foreign Guest at our meeting only two years ago, died on Sept. 10, 1947.

It is safe to say that no president of this Society has ever embarked on the preparation of his annual address without calling into consultation all the long line of his predecessors, through a review of all the presidential addresses of past years. Incidentally, such a review is highly educational, and it might well be made a required course of reading for all future presidents.

Just as much of the world's history consists of such periodically recurring events as wars, scientific discoveries, and religious upheavals, so have many of the fundamental problems of our specialty been with us since the founding of the Society and the address of our first President, Fordyce Barker. Much of this old wine has been put into new bottles by many of his successors. If it is true, as Sir Thomas Browne said, "that in seventy or eighty years one may have a curt epitome of the whole course of time," no president of this Society need go any further in his search for ideas than the addresses of his predecessors, especially if he feels no qualms at a bit of genteel plagiarism. For this he will have high moral support, for no less an authority than Emerson has said that "it has come to be practically a sort of rule in literature that a man, having once shown himself capable of original writing, is entitled thenceforth to steal from the writings of others at discretion."

In scanning previous presidential addresses, I have been interested to note how differently our presidents have interpreted their constitutional obliga-

tion to deliver an address at the annual meeting. Some have seized the opportunity to read papers on very specific scientific subjects in which they themselves were especially interested, with probably a fiendish glee that for once their remarks would not be curtailed by the sharp tap of the gavel made from Ephraim McDowell's door knob, always ruthlessly closing and never opening the door for prolonged discussion. This is a contribution of Ephraim McDowell which has never been sufficiently appreciated. Such a conception of the presidential address as I have described appears to be a rather selfish one, simply adding just another paper to an already heavily laden scientific program, without even the redeeming feature of the time limit imposed on other essayists.

Not a few of our presidents have chosen to devote their addresses to historical accounts of great events, great movements, or great personalities in the development of our specialty, and certainly no criticism can be made of the interest and the cultural value of such presentations. The same may be said of the few addresses which have gone rather far afield from our specialty into the realms of general science or literature.

The majority of past addresses, however, have been of general and composite nature, so much so that they have no titles, going down in our archives simply as "Presidential Addresses." They have dealt with all manner of topics of current interest and importance to the Society and the specialty, such as medical education, the proper training of those aspiring to be specialists, discussion and criticism of policies and trends, recommendations for the future, etc.

It is this concept of the presidential address which appeals to me as the logical one, the one intended by our Founders, and the one which might be expected to serve a real purpose, above that of a mere formal embellishment of our annual meetings. Such a concept would make the address similar in purpose to the annual Report to Congress by the President of the United States on the State of the Union.

If a title were insisted upon for such a simple and homely discussion of family matters, a tempting one would seem to be that of "A Fireside Chat," to borrow a designation made famous by the now silent golden voice which flowed so seductively over the ether waves only a few short years ago. I would, however, have to disclaim some of the original connotations of this term, for in our own small circle there have been no real or imaginary crises, there are no economic royalists to vituperate, and politics has never reared its ugly head in our midst.

But we have had our little family problems, and these should have made some impression upon those of us who have enjoyed Fellowship for many years. An address of this sort should, therefore, afford the President the opportunity of getting off his chest his reaction to some of the problems of the Society, although I must confess that I have nothing on my chest which has pained or oppressed me. While such pectoral purgations may be looked upon as largely excretory in nature, they may actually serve a fertilizing purpose, just as certain unmentionable excrementitious material may be transformed into the loveliness of a Chinese or Japanese flower garden.

I propose, therefore, to discuss a variety of topics, emulating the Walrus of Alice's Looking Glass, in the familiar lines:

> "The time has come, the Walrus said,
> To talk of many things;
> Of shoes and ships and sealing wax,
> Of cabbages and kings."

A useful recipe for the preparation of an address of this sort, and you will find it equally serviceable in the concoction of commencement addresses, extemporaneous after-dinner talks and other such purposes, would seem to call for the following ingredients:

1. A wise and well-tempered discussion of the various topics which have been selected for the body of the address;

2. A sprinkling of classical and literary allusions to indicate the breadth and depth of the speaker's cultural attainments, and

3. A dash or two of purported wit to lighten the profundity of the discourse. I am afraid that, like the corner groceryman, I am "just out" of some of the necessary ingredients, so that the resulting brew may leave something to be desired.

Each year our Society receives an invigorating infusion of new blood, through the election of a number of new Fellows, and it is the caliber of these new recruits which will determine the future standards of our organization. Our Council has no more important function than the careful screening of the candidates who come before it for consideration. The stated policy has always been the preliminary selection of a group of potential candidates who are then invited to participate in the formal program of the succeeding meeting. The latter is a wise provision, since it gives the opportunity of personal evaluation of possible candidates. However, it has always seemed to me that there are two possible points of weakness in our present method of procedure.

First of all, those who are formally listed as invited guests and potential candidates are usually nominated by individual Fellows. Certainly no Fellow should be deprived of this right of nomination, but the final selection of candidates should not, it seems to me, be limited to these individual nominations. The Council should be given the authority, which it does not now have, to go out into the open market, and this right should be exercised as a formal policy.

According to our present Constitution, candidates for Fellowship "shall be proposed to the Council by two Fellows only, who are not members of the Council, at least two months before the first day of the meeting, etc." This prerogative should be continued, but in addition, the Council should be privileged to bring to the Society's attention the names of other worthy candidates, who are easily overlooked if they do not happen to have a friend at court. It should be empowered to pluck the fairest flowers that bloom anywhere in the country, and not only those which happen to grow in some Fellow's backyard. It is easily conceivable that young men of great promise or of already proved accomplishment might never otherwise be brought to the Society's consideration.

"Full many a gem of purest ray serene
The dark unfathomed caves of ocean bear;
Full many a flower is born to blush unseen,
And waste its fragrance on the desert air."

Secondly, the introductory paper or discussion required of potential candidates should not be given undue weight in the consideration of the candidate's qualifications. Even the veriest neophyte, with such an incentive as possible Fellowship, might conceivably produce an outstanding contribution, and still fall short of proper standards for admission. By the same token, men who, by virtue of their teaching positions and their professional stature, were clearly qualified for Fellowship have on more than one occasion presented very undistinguished or even poor introductory theses. In the latter case, the Society as a whole has always, so far as I recall, recognized the Homeric nodding in such presentations, and has looked beyond them to the already demonstrated worth of the candidate.

Again, it should not often be necessary for our Fellows, in looking over our programs, to ask "who is this man who is reading a paper on such and such a subject?" Most of our candidates should be men who through their accomplishments and their publications have already stamped their names on our minds. Being now a member of the Council and knowing how conscientiously it guards the gateway of admission to the Society, I feel all the freer in making these comments.

It is gratifying that our Society has within recent years shown a tendency to admit to Fellowship an increasing proportion of comparatively young men who had already given clear indication of actual or potential leadership in our specialty, thus creating a healthy balance between the mental alertness, elasticity, and enthusiasm of youth on the one hand, and the maturity, balance, and allegedly greater wisdom of those no longer young. As the garrulous but lovable Autocrat said, "New ideas do not build their nests in old men's brains, and the first whisperings of truth are not likely to be heard by those who already feel the need of an ear trumpet."

On the other hand, it is more common in the young than in the old for the mind to function like a sponge, sopping up new knowledge indiscriminately, and giving it off in great profusion on the slightest squeeze. Without the slightest attempt at generalization, which would of course be ridiculous, the minds of more mature men are more likely to develop sievelike characteristics, sifting out the knowledge which can be actually utilized. This is another way of expressing the aphorism that "knowledge comes, but wisdom lingers." In any event, I do believe that our older men are likely to have lost a good deal of the charming credulity so characteristic of our profession, and to have developed some degree of healthy skepticism toward many of the superficial new ideas of one sort or another which each year brings. Some of these die a-bornin', some die quickly and are soon forgotten, but still others may get such a foothold that many years are required to dislodge them.

The above remarks will be put down, probably correctly, as the prejudiced ramblings of one who can no longer consider himself young. They started off

quite innocently with the simple observation that our Society represents a happy mixture of the young and those not so young, that we shall have to depend upon the former to carry our standards into the years of the future, and upon the latter to act in a steadying and comforting capacity, like the convenient scratching-boards which give solace to the cattle in the pasture. To put in a final lick for my older colleagues, they may, at any rate, like peaches or bananas, be expected to become mellowest and sweetest before they decay.

In the scientific world, as in the social world, the oldsters might just as well reconcile themselves to the fact that they must, in their own clumsy and creaking fashion, adapt themselves to the ways of the younger generation among us, and not vice versa. During the restless years between the two World Wars, many an anxious parent had serious misgivings as to the fate of the youngsters of those days, who succumbed so easily and often so enthusiastically to the temptations of cocktail parties, who in their dancing hours took up where their parents left off, and who dashed about the countryside in fancy roadsters or collegiate jalopies.

The later history of this particular young generation has shown conclusively, I believe, that our grim forebodings were not warranted, and that such fundamental American attributes as initiative, resourcefulness, and courage were not affected by such passing phases as I have mentioned. It was these very qualities in many millions of our young people which brought us safely through the recent war holocaust, and it is to them that we must look for the ultimate reconstruction of a brave new world from the battered old globe we are turning over to them.

In our own profession, however, and in the narrower field of our own specialty, the older generation need make no apology for the legacy it is leaving to its successors. Moreover, the older Fellows of this Society, raised in a purely clinical era, deserve much credit for learning the new vocabularies which have marked the development of our knowledge, especially in the fields of pathology and endocrinology, not to speak of the new fields of obstetrical immunology and chemistry.

It is my impression that the older members of our profession have found it more difficult to reconcile themselves to the changing order in medical education, and not a few continue as die-hards in this respect. In a not so remote day, the men on whom professorships were bestowed were those who had achieved clinical maturity and eminence, and who were ordinarily as mature in years as in experience. Such appointments now go to young men selected because of their scientific promise, which with much justice is considered a far more desirable asset than the more readily acquired clinical experience. There are many who still think that a happier compromise could be struck than has yet been reached, but the newer surge has become so strong that it cannot be gainsaid, and it will probably justify itself. In this respect, the older generation has bowed gracefully to the new order, just as it has accepted the closely related policy of full-time professorships, which for so long divided our profession, and which is still viewed with dubiousness by some in our ranks.

Not much more than a generation ago, the specialists in our own and other fields were largely self-trained, many of them entering the specialty through the gateway of general practice. This fact was recognized by the American Board of Obstetrics and Gynecology in its earlier years, and provision was wisely made for the certification of applicants thought qualified by years of practice in the specialty, even though they were lacking in the years of formal training now required of all candidates. No longer should a man expect to learn his specialty by the method of trial and error, as did the famous ophthalmologist who confessed that he had spoiled a whole hatful of human eyes before he perfected himself in the cataract operation.

The Board has made a notable contribution to the postgraduate training of obstetricians and gynecologists and to the elevation of standards of specialization in this field. It has no doubt made some mistakes, and it would be strange if all its policies and aims met with universal approval, but on the whole it is doing a much needed job and doing it well.

Having as an Associate Examiner assisted in the conduct of a number of the Board examinations, I have been deeply impressed with the unselfishness of the Board members in giving so generously of their time and effort in carrying on their really arduous work, and of the idealism and sincerity of the Board's purpose. It is not invidious to emphasize especially the long years of faithful service rendered by the Chairman of the Board, Dr. Walter T. Dannreuther, and the Secretary, Dr. Paul Titus.

Whatever the older men of the profession may think of the Board's work, although even these must now be convinced of its value, the young men throughout the country have made Board certification their first big objective after completion of their training. This has inevitably impelled them to seek their training in hospitals approved by the Board, and thus has immeasurably improved the quality of service in hospitals desirous of securing approval for postgraduate training in obstetrics and gynecology.

It is difficult, probably even for the Board itself, to prophesy its ultimate effect upon the development of our specialty, but few will doubt that it is moving in the right direction. It has publicly disclaimed any advocacy of a policy that Board certification be required of those holding senior hospital staff appointments, and yet just this policy has already been adopted by some of the hospitals in this country, with often resulting rancor and discontent among the staffs of such hospitals. Indeed, it is not rare to hear reports of discontent among residents because their chiefs are not Board diplomates, and one gets the impression that some hospital residency tenures are looked upon merely as opportunities for putting in the requisite number of years and cramming for the Board Examinations, rather than in broad and systematic training for the specialty. These are disadvantages which will in time correct themselves, and they do not, in my judgment, reflect upon the wisdom of the Board's fundamental goal of raising the standards of practice in obstetrics and gynecology.

The World War has greatly intensified a problem which had already been evident, that of the difficulty faced by young men who aspire to enter our specialty of obtaining opportunities for the special training required by the

Board. The simple fact is that there are not enough posts of this kind available to take care of the large number of deserving young men anxious to train themselves as specialists. This is true in spite of the helpful policy of a good many hospitals in increasing the size of their resident staffs. The condition will probably improve somewhat after the backlog of returning veterans has been taken care of, but the general problem will still remain. It has been necessary to make use of the preceptor system as a supplement to more formal training, but this is probably to be looked upon as a necessary but far from ideal makeshift.

The chief hope would seem to lie in an increase in the number of hospitals qualifying themselves for Board approval. As the number of Diplomates will steadily increase, and as these will in the future increasingly dominate the hospitals which they will staff, there is all the more reason to expect a steady increase in the number of hospitals offering a satisfactory type of training.

An even greater need for postgraduate instruction has become apparent in the past few years through the influx of large numbers of foreign physicians who are seeking postgraduate instruction in our clinics. The world leadership in medicine which Germany had so long held had been slipping from her grasp a good many years before World War II, but its fall was precipitate with the rise of Nazi power. Government-inspired studies in *Rassenhygiene,* always demonstrating the supremacy of the pure Nordic blonde, were sorry substitutes for the substantial and often brilliant scientific output which made the Germany of a preceding generation the Mecca of medical men from all over the world.

Leadership is now in our own hands, and there is little doubt that here it will remain for many years to come. We can well be proud of the accomplishments which have given American medicine this world supremacy, but if we are to be the teachers of the world, we must develop a much more elaborate machinery for postgraduate instruction than now exists. Many of our leading medical schools have had practically no machinery of any sort except that represented by the postgraduate training of hospital and resident staffs. Foreigners visiting our clinics are likely to be received courteously and they are made welcome to observe the work of the clinic, but without any attempt at formal instruction.

Such visitors are now flocking to us in ever increasing numbers, especially from the Latin-American countries, but with many also from both Europe and Asia. Many of them are satisfied with the crumbs which they can pick up by superficial observation of the work of perhaps many clinics, just as many Americans in a former day were content with similar superficial visits to the German medical centers. Even such visits as these had their value, if for no other reason than that they gave some idea of the atmosphere of the German clinics, and the opportunity of seeing and hearing some of the great masters of the German medicine of that day.

I am sure that a considerable proportion of the older men here present treasure the memories of such visits, and of having had at least some contact with such personalities as Bumm, Stoeckel, Meyer, Franz, the Landau brothers, Strassman and Ludwig Pick in Berlin, and with other such leaders as Schröder, Döderlein, Sellheim, Wertheim, Schauta, Halban, Menge and many others whose names will long remain in the literature of our specialty.

Such visits had a collateral cultural value, for the work of the American "student" was rarely taken so seriously that it interfered with sightseeing, visits to cathedrals and art galleries, and, last but not least, many delightful sessions in the very "gemüthlich" atmosphere of the fine beer gardens of all the German cities. These were often enriched by extracurricular discussions with the younger members of the teaching staff, always willing to give their all for a good meal and a few steins of beer.

On the other hand, it must be admitted that certain of the very poorly paid *privat-docents* were far more mercenary, giving of their knowledge only at so much per hour. This was only a reflection of the general European attitude toward Americans, all of whom were of course fabulously rich according to the European concept. Even in those days, the traveling Americans contributed generously to European economy, an American role which has been blown up to colossal proportions by the two World Wars. It would almost seem that two totally different words which sound alike, "succor" and "sucker," have come to mean about the same thing.

While perhaps the majority of American visitors to the German clinics of a former day belonged to this butterfly type, which flitted from clinic to clinic, taking dainty sips of whatever each one offered, there was a minority of more serious students who dug themselves deeply and for long periods of time into those clinics which could offer them what they wanted. One has but to consider the lives of such men as Welch, Halsted, Cushing, and a whole host of other American medical leaders to appreciate the full force of the German influence to which they exposed themselves in their formative years.

This German influence forever afterward colored the lives of these men, and through them and through the successive generations of men whom they themselves trained, it undoubtedly played an important part in the steady and rapid development of medical education in our own country. For example, I believe it can be shown that the Flexner report of 1910, commonly looked upon as marking the end of the era of proprietary medical schools and diploma mills and the beginning of the modern era in our medical teachings, stems directly from a group of men who were ambitious to emulate the then unexcelled German system.

We should not be ashamed to acknowledge this debt we owe to the German medicine of the pre-Nazi era, however much we may deplore its later débacle, and however much we may pity or even despise the German people, including many of our own profession, for their blindly enthusiastic participation in the Hitlerian orgy.

A review of the Transactions of this Society must impress one with the generally high standard of the hundreds of scientific papers embodied in them, and of the contributions which this Society has made to the literature of our specialty. On the other hand, it will probably be disillusioning to one who seeks for contributions which might be considered of epoch-making importance. In the nearly quarter century covered by my own active membership I can, as a matter of fact, think of only two contributions by Fellows of this Society which

would unquestionably be accepted as "outstanding advances," or, to use a much abused designation, "discoveries."

One of them is the important contribution of the late John A. Sampson in establishing pelvic endometriosis as an important and frequent pathologic and clinical entity. The other is the introduction of tubal insufflation by I. C. Rubin, representing as it does the most important advance of our generation in the study of female infertility. Even if one looks back over a much longer span, to the very inception of the Society, a similar paucity of really historic contributions is revealed. I hasten to add that this comment is not to be interpreted as reflecting on the scientific fecundity of this Society, but rather to impress the fact that, while the literary mills grind on in our specialty as they do in all fields of medicine, and while every year many papers appear which add scattered bits to our knowledge of obstetrics and gynecology, one can hope for only an occasional forward thrust of the frontier of knowledge of clear decisiveness and importance.

After all, discoveries cannot be pulled out of thin air. I have a friend, a distinguished scientist, with whom I occasionally had luncheon in his laboratory when he was in Baltimore, and who, when one o'clock came, would often pull out his watch and exclaim, "My goodness! Time to go upstairs and make another discovery!" Rarely does a discovery come crashing into the brain like a bolt from the blue. More often, it is the final culmination of the long and painstaking work of many years, not only on the part of the discoverer himself, but also of many other investigators in many lands and going back many years. Advances in knowledge are usually achieved by this building-block method, only the gleaming capstone being placed by the man whom the world acclaims as a genius. As Edison says, genius is composed of only about 2 per cent inspiration and 98 per cent perspiration. The really productive investigator must have imagination and vision, as well as the ability to sift out from the work of those who have gone before him the shiny fragments which denote rich scientific potentiality. But beyond this rare gift for selecting the direction of his own research, and perhaps it is this which constitutes the real "divine afflatus," there is then required a period of long and intensive effort which may stretch over many years.

The research man works with his problem, sleeps with it, and dreams of it, so that he becomes a veritable scientific monomaniac. To illustrate, once Sampson had gotten his teeth firmly into the endometriosis problem, all of his subsequent papers during the twenty-five years before his death dealt with the same disease, except for a small group on another subject, obviously stemming from his studies on endometriosis. In the same way, only a small proportion of Rubin's numerous papers since his introduction of tubal insufflation in the study of sterility, something like 10 out of 69, have dealt with subjects other than sterility and tubal insufflation. This does not by any means indicate that these men had single track minds, for both were men of broad gynecologic training, with an interest in all gynecologic problems. It means simply that concentration of effort was necessary for the establishment of the advances for which they are responsible.

Many sins are committed in the name of research, the desirability of which we are constantly preaching to our younger men. Laudable as this inspirational propaganda is, it no doubt explains the enormous annual spate of mediocre publications, since many appear to have the naive idea that writing and research are more or less synonymous. The dictionary definition of research as a "critical and exhaustive investigation or experimental study having for its aim the discovery of new facts and their correct interpretation," indicates that it is made of much sterner stuff.

Only a small fraction of medical papers represent true research, and yet the fact remains that a large proportion of them serve a valuable purpose in refurbishing established knowledge in newer or more attractive or more forceful form, and every pedagogue knows that reiteration is an indispensable asset of good teaching. In a broad sense, such publications can be considered a very important part of the postgraduate training of both the author and the reader. No one profits more from a paper than the author thereof. There is much truth in the old saying, "if you don't know anything about a subject, write a book about it." The only trouble is that sometimes readers of such books lay them down with the feeling that the author still knows very little about his subject.

The longest journey begins with a first step, and the first literary step may be halting and uncertain. It may take the form of case reports, and even those are not always to be scoffed at. Or the young author may very early show a statistical bent, though this is not likely to result in papers of great glamor. This statement probably expresses a personal prejudice on my part, since, with full appreciation of the value of statistics of the proper sort, I happen to be one of those handicapped individuals who shudder at the sight of long columns of figures, plentifully interspersed with decimal points and even an occasional logarithm, and who grow dizzy following the ups and downs of the beautiful graphs adorning many of these statistical papers. Still others of the neophytes early show an interest in the pathologic, or the chemical, or the bacteriologic, or the radiologic aspects of their work, and such early interests are not infrequently indicative of the later special professional interests of such men, as amply illustrated in our own Society.

It is only natural that most of those who write on gynecology and obstetrics in our country seek an outlet in the only American journal of national scope devoted exclusively to our specialty, and the able editor of that JOURNAL is hard put to it to find space to take care of this output without unreasonable delays in publication of his material. But it would not be fair for the editor to be too hardboiled in the rejection of papers just because they do not show impressive originality or because they emanate from men whose names are as yet unknown to us. Often they are young men just trying their literary wings, and they deserve the encouragement which they get when they see their names in print for the first time. Among them will be some of the future leaders of our specialty. While this problem of providing proper outlets for the ever increasing literature of our specialty has been the subject of considerable discussion, and while it has also been considered by your Council, the feeling has been general that the official organ of our Society has, under the long and able editorship of Dr. George W. Kosmak, rendered an outstanding service to our specialty.

To revert for a moment to the subject of medical research, there are other aspects which have disturbed a great many of us. In his address at the opening of the Banting Institute in 1930, the late Lord Moynihan stirred up a hornet's nest by lamenting the fact that so much of the research carried on in medical institutions is directed to problems which can scarcely be considered to have any bearing on human health and disease. He also bemoaned the fact that mice and rats received too much attention from investigators, and that too little is given to the human being who, after all, is a very readily available animal suitable for at least some types of experimental study.

It is obvious that hominal research, as Moynihan called it, has very sharp limitations, even though there is some reason to feel that it has not been as richly developed or as highly organized as has been the experimental laboratory study of the lower animals, which has yielded so large a proportion of the really outstanding advances in medical science. It is easy to understand the rather violent reaction created by Moynihan's criticism among those working in the field of medical research, although it may still be true that those working in medical research laboratories do not devote a sufficiently large proportion of their efforts to problems with clearer and richer potential application to human health and disease.

There are other so-called "researchers" who appear to delight in setting up men of straw and then knocking them down with great gusto. They spend much time and money in proving figuratively, that the moon is not made of green cheese. The world's reaction is likely to be "Cui bono?" which, in loose translation to good American slang, would be, "So what?"

These somewhat flippant comments are made simply to emphasize the fact that not all research is intelligently conceived or prosecuted, and that a considerable fraction of it is of that spurious brand to which our late enemies, the Germans, applied the expressive designation of "*Scheinwissenschaft.*"

No one has more beautifully allegorized the never-ending quest for truth than Milton, who relates that the lovely form of the virgin Truth was hewn into a thousand pieces and then scattered to the winds. Since that time mankind has been searching for these fragments in all corners of the earth and in all fields of science. Those fragments bearing on human health and disease are most likely to be discovered by medical investigators, just as physicists and chemists are more likely to find the fragments bearing on their own sciences. But there is no law against the trade and barter of fragments when these can be better utilized in other fields. To mention the most outstanding example, the discovery of radium by the Curies, in the field of physics, has been the means of saving many lives when applied in the field of medicine.

It would be tempting, if time permitted, to discuss some of the important clinical problems with which our specialty is concerned, and especially that of cancer, still the ruthless destroyer of so many of the women committed to our care. Suffice it to say that now, and for the first time, the warfare against cancer has assumed all-out proportions. Not only our own profession, but scientists in every other field are now enlisted in the cause—pathologists, chemists, endocrinologists, physicists, botanists, and geneticists. Nothing is more certain than that

the riddle of cancer will be solved, possibly in the not-too-distant future, and it is even possible that a cure will be discovered before the cause of the disease is revealed.

In the meantime, substantial if not brilliant gains in the salvage from the disease have been made by both radiotherapy and surgery. Most of us must feel that both of these, in spite of their accomplishments, are to be looked upon as make-shifts, often effective, until some more specific plan of treatment is discovered, something comparable in the life-saving field to the atom-bomb in the destruction of life, though not necessarily, of course, related to the application of atomic energy. If I were anxious to perpetrate a particularly pernicious pun, I could say that the salvation of the daughters of Eve does not necessarily depend upon the behaviour of an atom.

The limit of membership in our Society was originally fixed by our Founders at sixty, and it was not until the presidency of J. Marion Sims in 1880, and at his instigation, that this limit was raised to one hundred, where it remains today. From time to time one hears the criticism that it is too low, in view of the enormous increase in the number of those now specializing in obstetrics and gynecology. I do not believe that this argument is sound, or that it would appeal to many members of our Society. If the number of specialists has greatly increased, so has the number of special societies, national, regional, state, and local. No man of merit can justly complain of the lack of a forum.

The fact that hundreds of obstetricians and gynecologists will never attain Fellowship in the American Gynecological Society indicates no snobbishness on the part of the latter, and no lack of receptiveness to those who loom clearly above their fellows. By the very nature of the stated standards of this Society, it must be an exclusive organization, using this term in a scientific and not a social sense. Furthermore, a much larger membership would mean the end of the pleasant and intimate gatherings which we now enjoy, usually under one roof, and in extremely agreeable surroundings. And it is just this intimate personal contact which is an outstanding charm and asset of our meetings. This would be sacrificed in the more hurly-burly type of meetings which a much larger attendance would entail.

On the other hand, I do believe it is always desirable to keep our meetings open to a limited number of guests, above those formally invited to participate in the scientific programs as potential candidates. A total attendance of two hundred or perhaps somewhat more would not rob our meetings of any of the advantages mentioned above, and it would extend to our guests the opportunities for personal contacts which have been stressed. A scientific paper can be read if it is not heard, but a hearty handshake, a game of golf, a pleasant and intimate chat at the luncheon table or in the rathskeller, all these involve close personal relationships far more indelible than the written word alone. It was Woodrow Wilson who said "I would never read a book if it were possible for me to talk half an hour with the man who wrote it." I shall always treasure the memories of the personal contacts and the friendships with many of the great men of our specialty which were made possible to me by our annual gatherings.

One need not need be a hero-worshipper to derive a thrill from the mere touch of the hem of the garment of greatness. The man who saw Lincoln and who heard his Gettysburg Address remained thereafter a rather hallowed individual. After all, the things which make a man great are not merely what he writes, but also how he lives, thinks, reads and feels. What he writes may live after him, and make him great in the eyes of the world, but the other traits too often are interred with his bones, though they may explain his greatness to those who knew him when living.

The end object of most men's lives is happiness, but there are wide individual differences in their concepts as to what constitutes happiness. To some it connotes wordly success, and the common fate of these is disillusionment. No work of art has ever impressed me more than a small bronze statue by the great Rodin in one of the galleries in Paris. It was, as I recall it, entitled Success, and it represents a man toiling up the steep side of a mountain. His haggard, tired face has just reached the top, and there he sees before him, the fruit of success, a pile of dead men's bones and ashes.

There are others who deliberately seek fame and greatness, forgetting, as our own John Hunter said, that "no man who wanted to be great ever was a great man." That most delightful of epigrammatists, Oscar Wilde, put it even more neatly when he said that "there are only two great tragedies in life, not getting what you want—and getting it!" It is what we see and do and feel during the whole journey of life that counts, and not the mere goal, just as the traveler gets his joy out of the scenery and the people he encounters rather than in merely reaching a certain destination. "To travel hopefully is better than to arrive."

It may seem like a profligate doctrine to urge that the greatest happiness and the greatest chance for real success is likely to come from living each day for itself, with not too much thought of the morrow, as Sir William Osler was so fond of preaching. If one has found a niche in life which he enjoys, as is true of practically all medical men, and if he is happy in his home life, his family, and his friends, he will accumulate a vast capital of happiness during his lifetime, and incidentally a modest or a great measure of what the world calls success.

Since I have, in keeping with my duly announced plagiaristic policy, borrowed a thought from the philosophy of William Osler, it may not be inappropriate to conclude this address with a fuller quotation from that beloved physician as to his ideals of life. Incidentally, I would commend this to you as a more realistic expression of the lofty ideals of our profession than is found in the archaic Hippocratic oath which has been repeated mumblingly by so many generations of medical graduates.

"I have three personal ideals. One to do the day's work well and not to bother about tomorrow. The second ideal has been to act the Golden Rule, as far as in me lay, toward my professional brethren and toward the patients committed to my care. And the third has been to cultivate such a measure of equanimity as would enable me to bear success with humility, the affection of my friends without pride, and to be ready when the day of sorrow and grief comes to meet it with the courage befitting a man."

THE PRESENT-DAY STATUS OF NONINVASIVE CERVICAL CARCINOMA*

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FOUR years ago we[1] presented before this Society a paper which concerned itself with the minimal histologic changes in the cervical biopsy which would justify a diagnosis of carcinoma. Our observations followed those of Schottländer and Kermauner,[2] who noted a thin layer of carcinoma extending over the surface, surrounding advanced cervical cancer. They also followed the epochal work of Schiller,[3, 4] who first conceived the idea that surface carcinoma could be the beginning of invasive cancer. He described many cases without evidence of invasion in which cellular changes in the surface epithelium were found that were identical to those of invasive cancer. When we undertook our study it appeared to us that there was not sufficient evidence in the literature to justify completely the belief that these intraepithelial changes were precursors of invasive cervical carcinoma. To elucidate this point, we made a comparative histologic study of the biopsy specimens showing malignant changes in the surface epithelium and the ultimate specimens of the cervices removed at hysterectomy. The cervices were cut into several blocks and sections made from different levels in a search for evidence of invasion. In fifteen of the sixteen cervices removed, histologic evidence of invasion was found.

Since our publication of 1944, we have continued to collect histologic and clinical evidence concerning this subject and it would seem that we have amassed sufficient data to crystallize our ideas on diagnosis and treatment. This paper is presented before this Society to give our conclusions based on a much wider experience and also with the hope of stimulating discussion concerning this subject.

The histologic picture of "intraepithelial carcinoma" or "carcinoma in situ" has become reasonably familiar to all those interested in gynecologic pathology. Figs. 1 and 2 are typical examples. There is a loss of normal stratification of the epithelial cells, variability in the size and shape of the cells, nuclear hyperchromatism, and a frequency of mitotic figures. In short, the cellular changes are identical to those of invasive cancer and, indeed, metastatic cancer. Schiller has described an abrupt, oblique line of demarcation between this abnormal surface epithelium and the normal stratified epithelium. Although we have seen such an oblique line (Fig. 3) many times, we have also seen an abrupt perpendicular change (Fig. 4) and the transition from abnormal to normal cells is often gradual.

Our observations lead us to believe that cervical carcinoma begins in the basal layer of the portio vaginalis and that slight changes in this layer may be the precursor of intraepithelial carcinoma. We have seen repeatedly in biopsy

*Read at the seventy-first annual meeting of the American Gynecological Society, Williamsburg, Virginia, May 24 to 26, 1948.

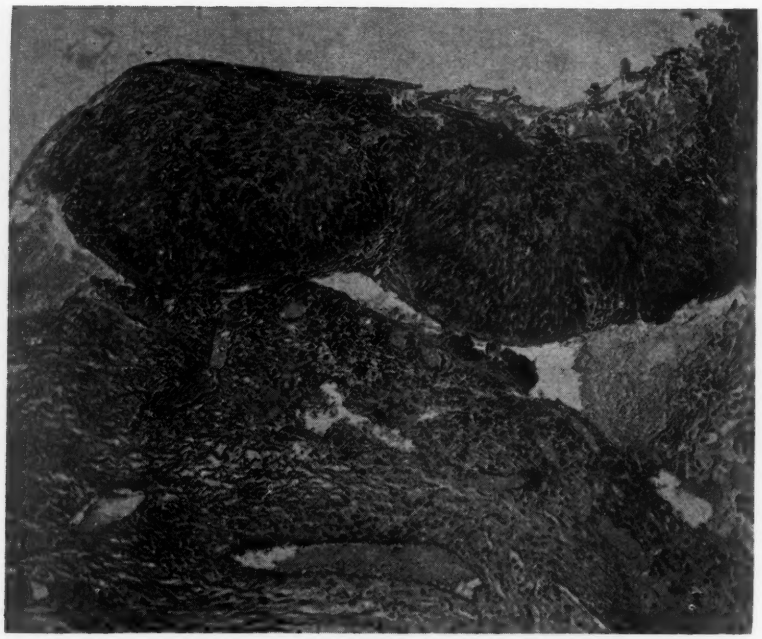


Fig. 1.—Path. No. 56452. Typical intraepithelial carcinoma.

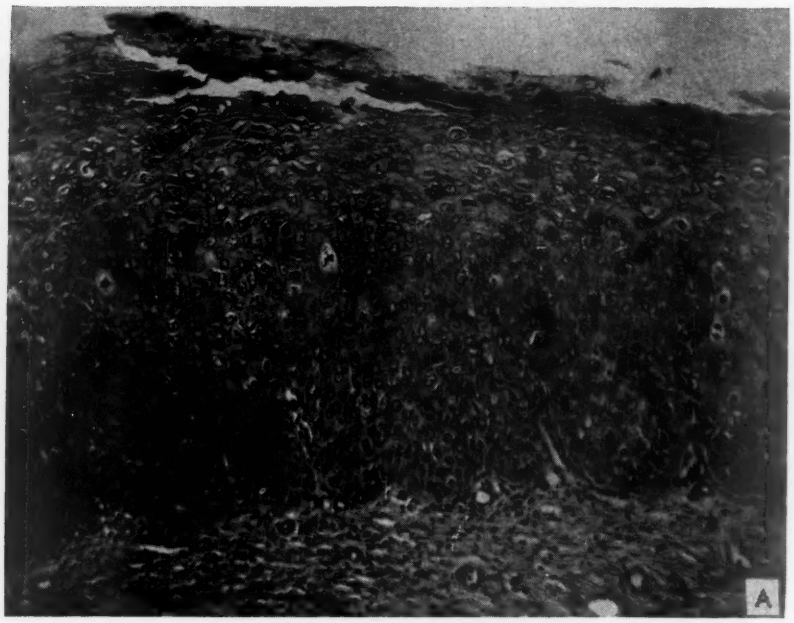


Fig. 2.—Path. No. 59392. Typical carcinoma in situ.

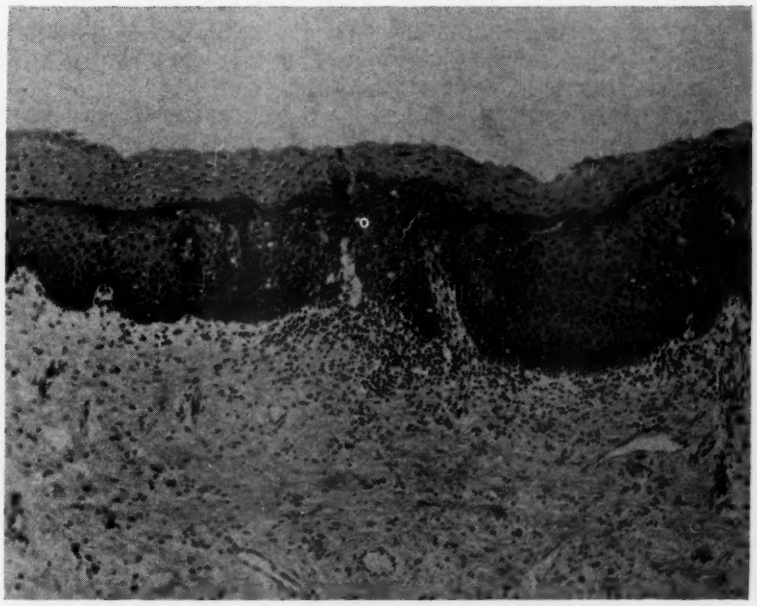


Fig. 3.—Path. No. 54078. Oblique line of demarcation between abnormal and normal epithelium.

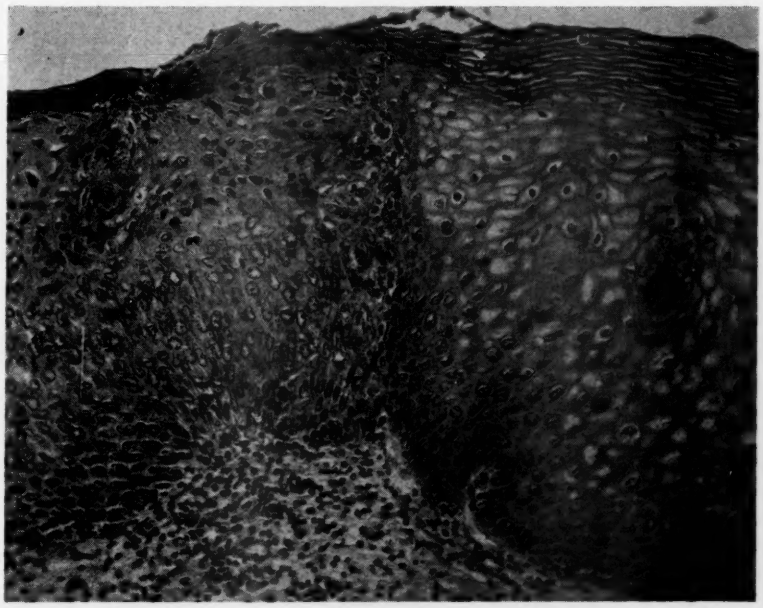


Fig. 4.—Path. No. 75417. Demonstrating an abrupt perpendicular change between abnormal and normal epithelium.

specimens changes in the basal portion of the surface epithelium which we interpret as basal-cell hyperactivity and for want of a better name we have designated these changes as such (Fig. 5). There appears to be an active proliferation of the dark hematoxylin-stained basal cells. These cells possess hyperchromatic nuclei and a varying number of mitotic figures. In the removed cervices we have frequently seen this activity of the basal cells adjacent to typical intraepithelial carcinoma and invasive cancer. All gradations of basal-cell hyperactivity are seen until the entire thickness of the epithelium is taken

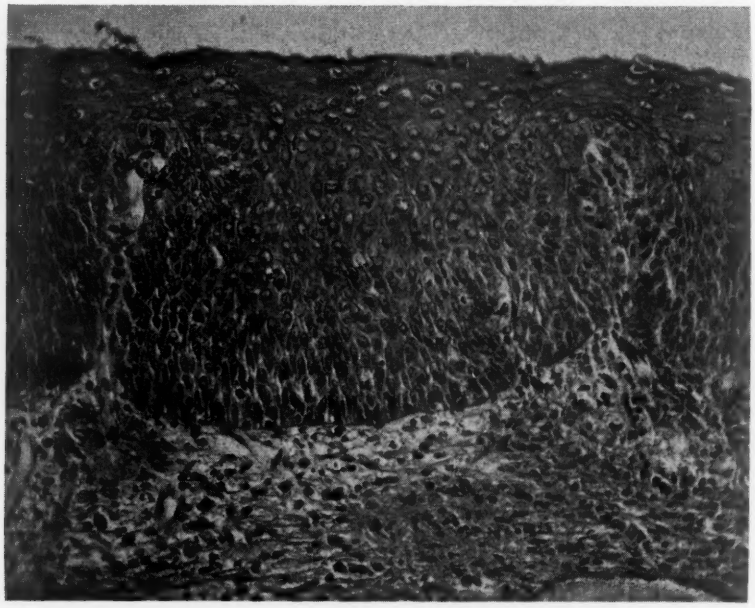


Fig. 5.—Path. No. 72800 . Basal-cell hyperactivity.

over by it, when the picture becomes identical to carcinoma in situ. As this hyperactive basal epithelium pushes upward, it may be sharply demarcated from the normal epithelium above or, more commonly, the abnormal and normal epithelium may blend gradually. We have observed basal-cell hyperactivity blend into full blown intraepithelial cancer so frequently, histologically, that we have become deeply concerned about its significance. The unanswered questions which have arisen in our minds are:

Does intraepithelial cervical cancer always begin as basal-cell hyperactivity?

Does basal-cell hyperactivity always progress inot intraepithelial cancer?

May basal-cell hyperactivity remain constant indefinitely or may it sometimes regress?

Histologically, there is a strong suggestion that basal hyperactivity does on occasion mature into carcinoma in situ but it cannot be stated with certainty that this occurs. The following case illustrates the possible progression:

The first biopsy was taken on Jan. 8, 1947, and showed only basal-cell hyperactivity (Fig. 6, *A*). A second biopsy was taken on Jan. 20, 1947, and again showed basal-cell hyperactivity (Fig. 6, *B*). A third biopsy, taken on Oct. 9, 1947, showed full blown intraepithelial cancer and on the basis of this finding a panhysterectomy was done (Fig. 6, *C*). When the cervix was sectioned, invasive cancer was finally found (Fig. 6, *D*).

On the other hand, on several occasions we have biopsied cervices and found definite basal-cell hyperactivity and repeated biopsies over months of time have shown only further basal-cell hyperactivity or no abnormality at all.

From a practical point of view we have regarded basal-cell hyperactivity as a warning, calling for repeated biopsies until such time as one can be convinced histologically that carcinoma does or does not exist. It is in these cases that we have often resorted to a cervical conization, done with a scalpel and followed by an electrosurgical conization to control bleeding. The cone of tissue is cut into several blocks and sectioned. By this procedure one can usually feel quite certain in establishing or ruling out carcinoma.

Whatever the final answer may be concerning the relationship of basal-cell hyperactivity to carcinoma in situ, the more practical problem today concerns itself with the relation of intraepithelial cancer to invasive cancer. Since the beginning of our study in 1940, we have diagnosed carcinoma in situ from biopsy 75 times. In some of these biopsies suggestive or slight invasion of the subepithelial tissues was noted but in all instances the changes in the surface epithelium were typical of carcinoma in situ. In 67 instances, we have performed a modified Wertheim operation for this condition. In one instance, the lesion was discovered in a cervix amputated in the course of a Manchester operation. In the remaining seven cases, conization of the cervix was done before radium was applied. Hence, in a total of 75 cases we have had the entire cervix or a generous cone for complete sectioning. In 55 instances, we found microscopic invasion. It is extremely difficult to put into descriptive terms one's criteria for invasion. We have, therefore, pictured here sections of several typical biopsies showing carcinoma in situ and sections of the corresponding cervices showing what we consider to be invasive cancer (Figs. 7 and 8). In ten cases in which the biopsy showed carcinoma in situ, only carcinoma in situ was found in the removed cervix and in ten instances no abnormality was found in the removed cervix, the entire lesion having possibly been removed at biopsy.

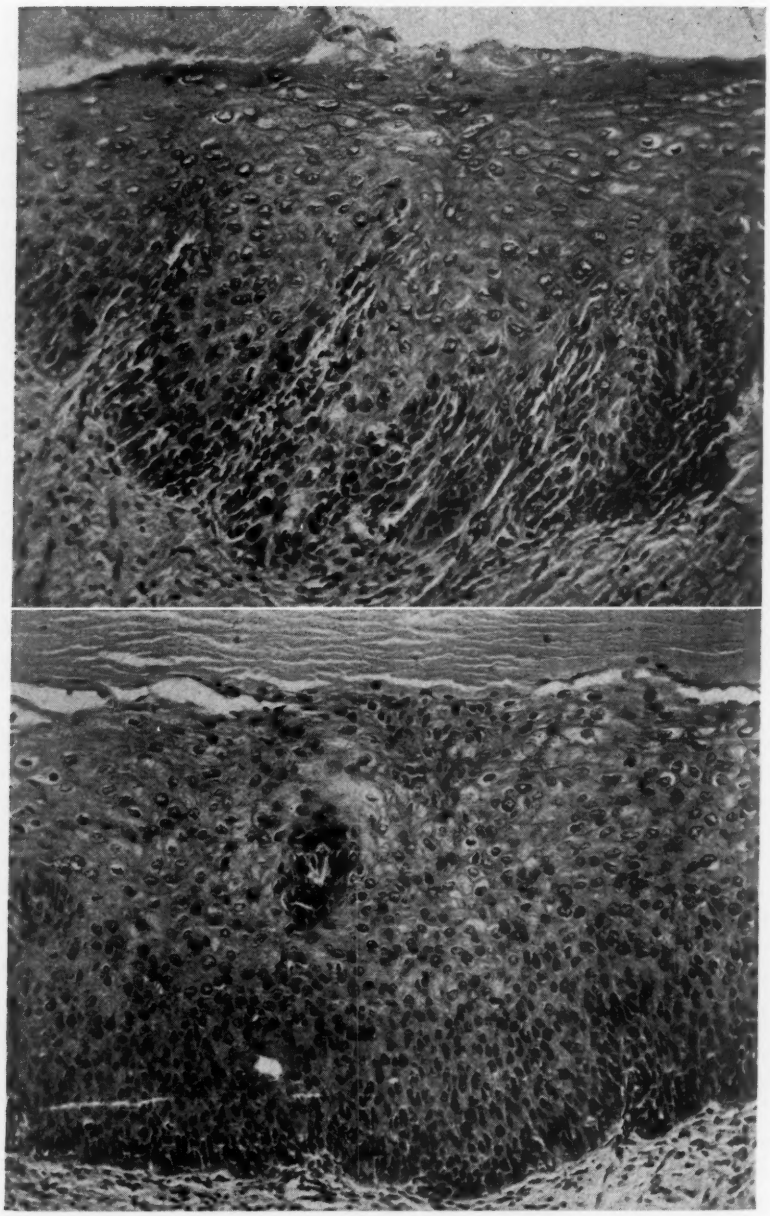
In order to study further the relation between carcinoma in situ and invasive cancer, we have made sections through the entire lips of several cervices. These sections are pictured in low power in Figs. 9 to 11. High power magnification of selected portions of these sections show typical surface cancer and the plugs of invasive cancer lying well beneath the surface. It is noteworthy that the plugs of invasive cancer in these sections are found at a considerable distance from the rather extensive surface cancer in situ.

From these studies it would thus appear that carcinoma in situ or intraepithelial carcinoma should be considered strictly as a histologic diagnosis and be regarded as indicating one of three clinical possibilities:

1. That the biopsy has been taken from the periphery of an advanced cervical cancer as was originally described by Schottländer and Kermauner.
2. That microscopic invasive cancer is present elsewhere in the cervix as was the case in 55 of our 75 cases.
3. That only carcinoma in situ is present and no invasion has as yet taken place. This was found to be the case in 20 of the 75 cases which we studied.

Therefore, in evaluating each case clinically the gross appearance and feel of the cervix should be considered. If, for example, a biopsy shows only carcinoma in situ but the gross appearance of the cervix is suspicious of more advanced cancer, more biopsies or, in some instances, a sharp conization should be done to evaluate the extent of the entire lesion. This, we believe, is of particular importance because of our views on treatment which will be discussed later in this paper.

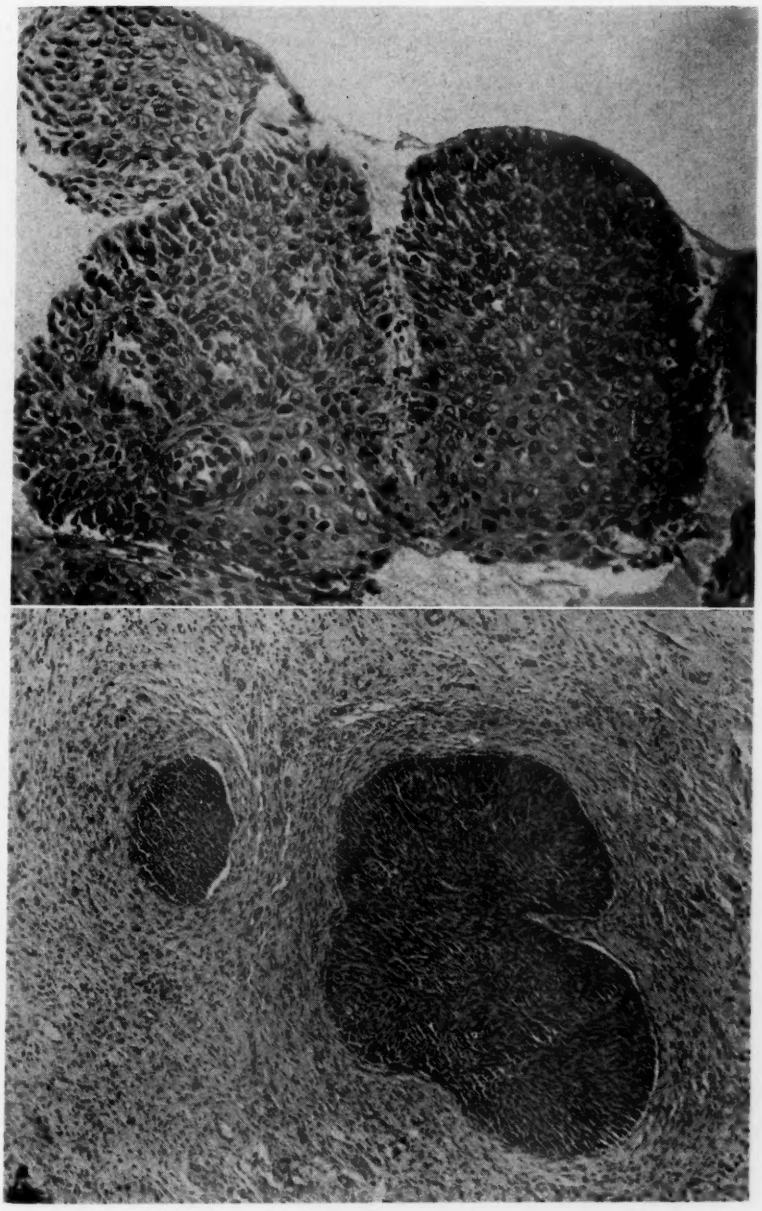
A.



B.

Fig. 6.—*A*, Path. No. 68601. Biopsy taken Jan. 8, 1947, showing only basal-cell hyperactivity. *B*, Path. No. 68877. Second biopsy taken Jan. 20, 1947, again showing only basal-cell hyperactivity.

C.



D.

Fig. 6.—*C*, Path. No. 72865. Third biopsy taken Oct. 9, 1947, showing intraepithelial cancer. *D*, Path. No. 73165. Showing plug of carcinoma in the depth of the removed cervix.

In formulating our concept concerning the relation of carcinoma in situ to invasive cervical cancer, a survey of the more important reports in the literature should prove valuable. It is well known that the curability rate has been high with various types of therapy. For the moment, we are not concerned

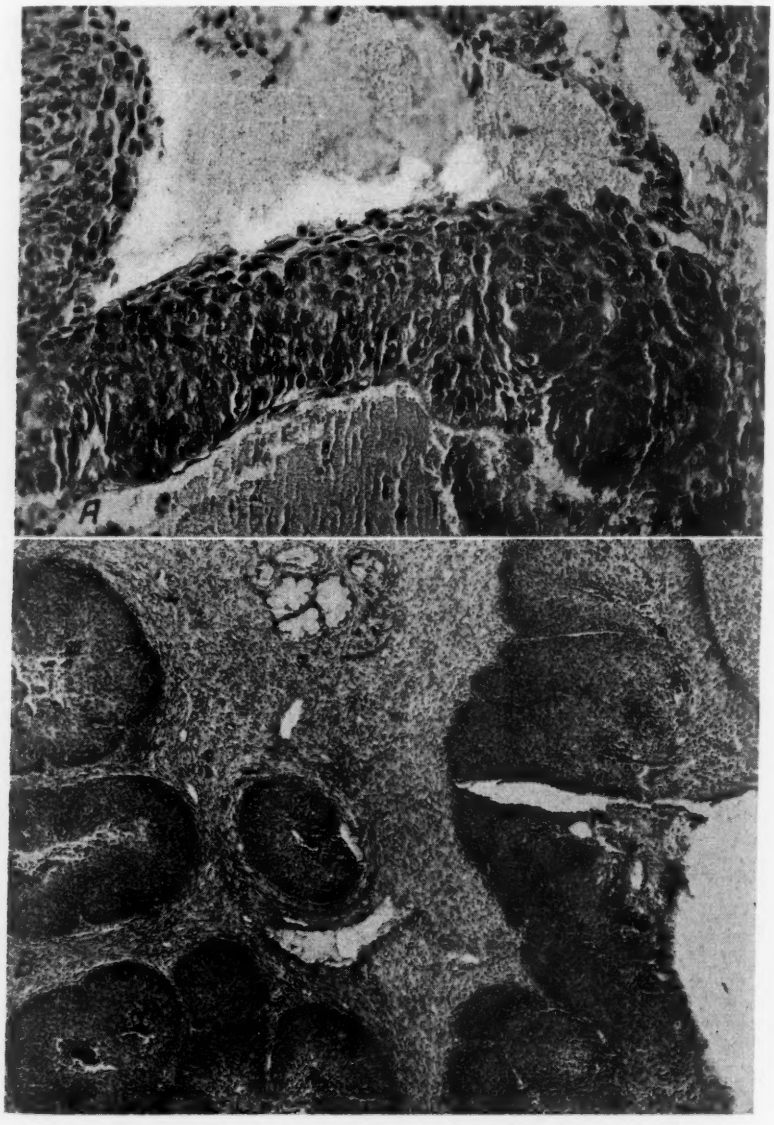


Fig. 7.—*A*, Path. No. 74370. Biopsy showing only intraepithelial cancer. *B*, Path. No. 74454. Section of removed cervix showing invasive cancer.

with that but rather with the ultimate fate of those patients who were not treated or who failed to be cured in spite of treatment. It is this group which will cast most light on the question of malignancy of these lesions.

Schiller[5] has reported one recurrence after five years and two recurrences before the lapse of five years following hysterectomy.

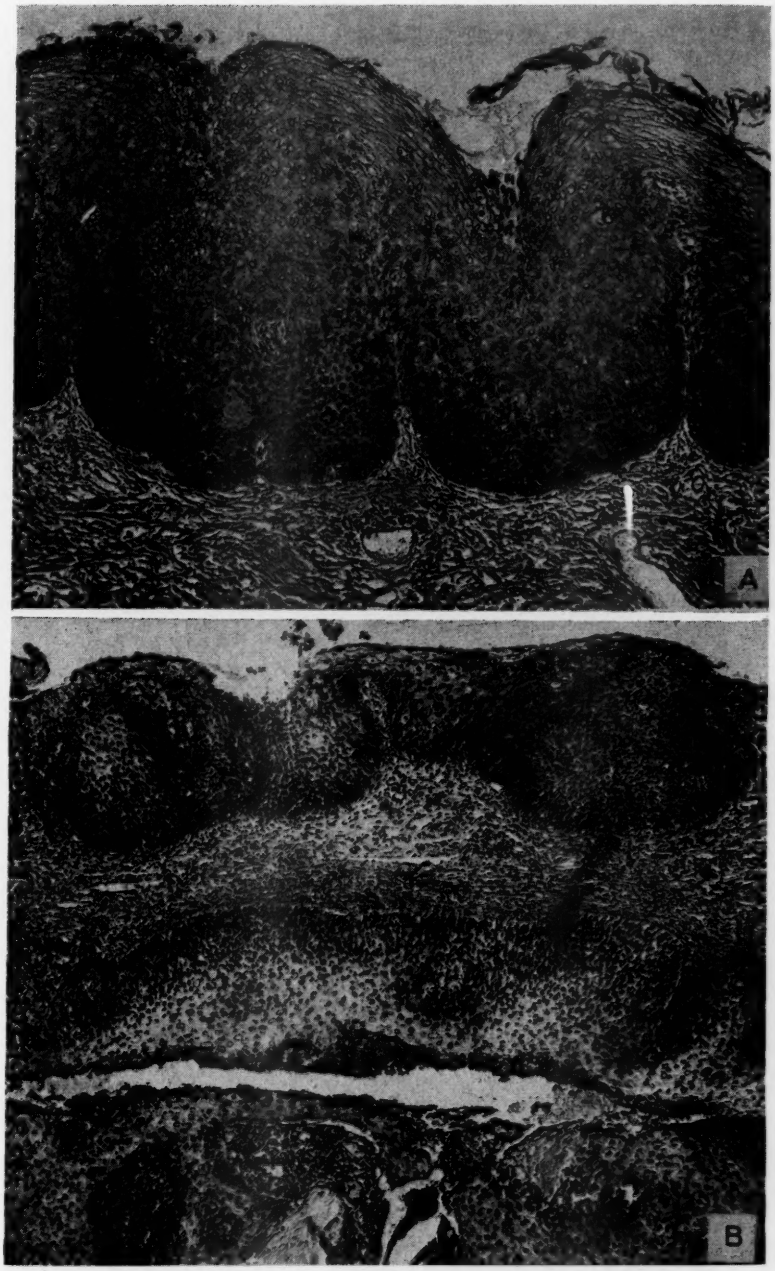


Fig. 8.—*A*, Biopsy showing carcinoma in situ. *B*, Path. No. 54078. Section showing intraepithelial cancer and invasive cancer in removed cervix.

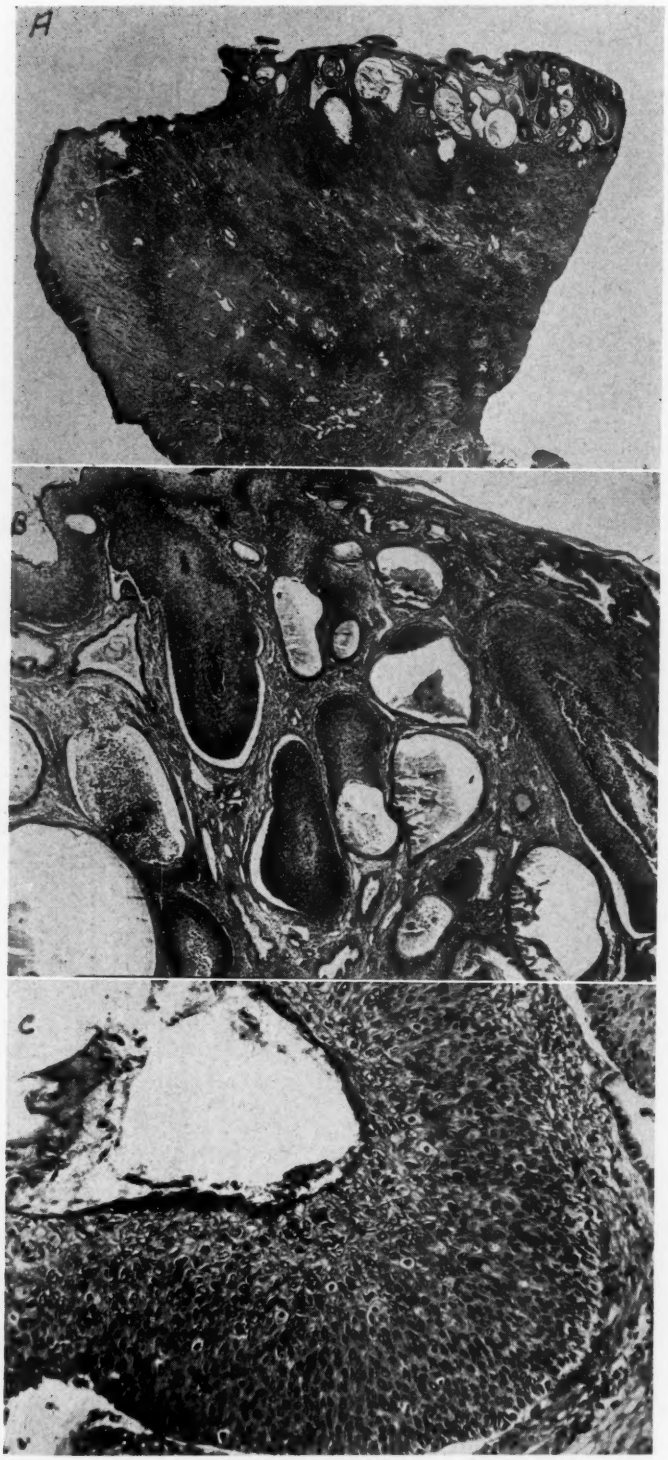


Fig. 9.—Path. No. 62339. *A*, Low-power section of entire lip, showing normal surface epithelium, carcinoma in situ, and invasive cancer. *B*, Medium magnification, showing invasive area. *C*, High power, demonstrating cellular changes.

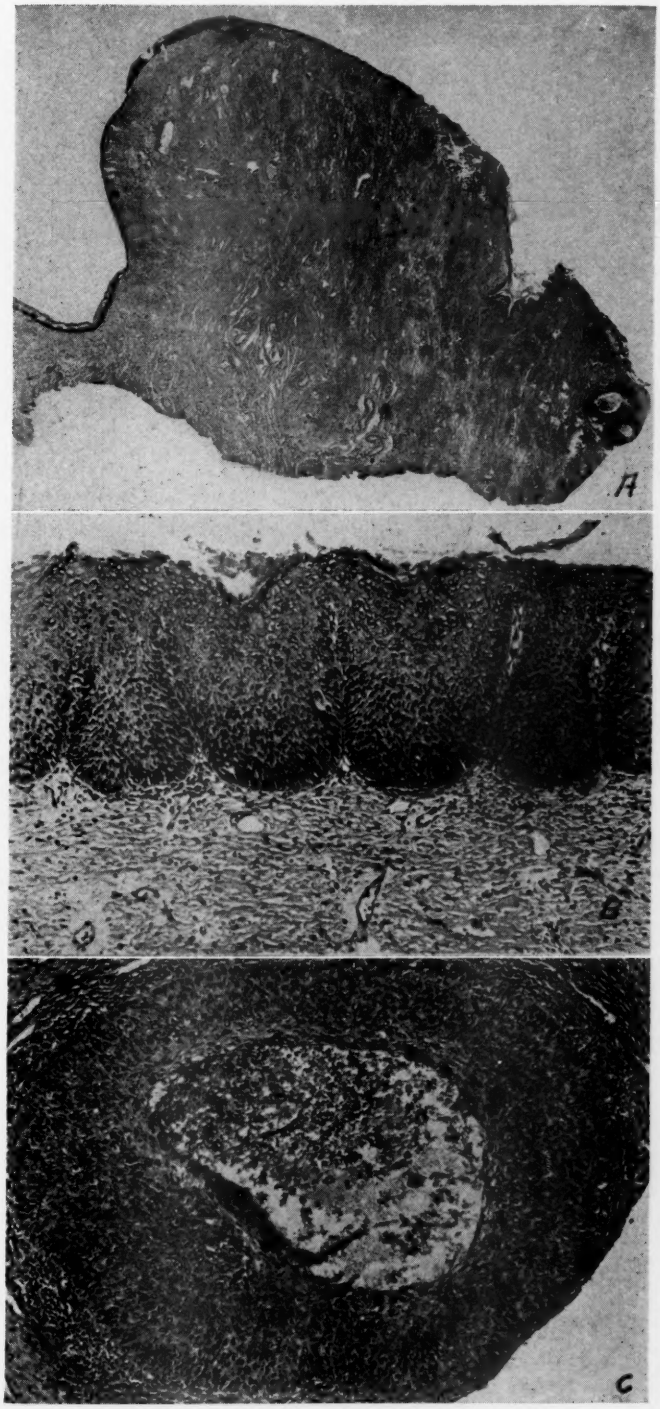


Fig. 10.—Path. No. 65809. *A*. Low-power section of entire cervix. *B*. Surface epithelial changes, higher power. *C*. High power of plug of invasive cancer. Note distance of this plug from surface cancer.

Stevenson and Scipiades[6] reported one case in which carcinoma in situ was present in a bit of tissue removed at trachelorrhaphy. This was not recognized in 1919. Two years later the cervix appeared normal on speculum examination. Nine years after the trachelorrhaphy the patient presented herself with an advanced cauliflower-like cancer of the cervix. A second case reported by them was that of a woman on whom a biopsy showed typical intraepithelial carcinoma. She died of another cause three and a half years later. Although she had never had any symptoms of cervical cancer, the sectioned cervix was riddled with invasive cancer.

Pund et al.[7] have recorded an untreated case in which advanced carcinoma was found four years and nine months after the initial biopsy, which showed only carcinoma in situ.

Smith and Pemberton[8] reported four cases in which tissue removed by biopsy or trachelorrhaphy showed intraepithelial cancer and in which clinical carcinoma was discovered four years and nine months, six years and one month, twelve years and six months and four years and one month, respectively, afterward.

Schmitz and Benjamin[9] reported one untreated case in which invasive cancer was found nine months after the in situ lesion was discovered.

Knight[10] reported one case which ended fatally three years after treatment by irradiation. Another of his cases was found to have invasive cancer four years and eleven months later.

Younge[11] reported invasive cancer developing in two cervices two years and two months and three years and four months, respectively, after biopsy.

Taylor and Guyer[12] reported one untreated case in a patient in which clinical cancer appeared seven years after the proved existence of carcinoma in situ.

One of our patients on whom only irradiation therapy was used died six months after the discovery of the in situ lesion. The autopsy showed metastatic cancer.

We have cited these cases somewhat repetitiously in an attempt to bring forth authentic clinical evidence to show that in at least 17 cases clinical cancer has followed pre-existent intraepithelial cancer. It is evident that clinical cancer may not make its appearance for many years after the known existence of the surface lesion. On the other hand, our own case terminated fatally after only six months. Such rapid progress is probably exceptional.

The age of these patients as compared with that of clinical cancer confirms our belief that the surface lesion may be relatively dormant for years before blossoming forth as clinical cancer. The average age of our 75 women with cancer in situ was 37.1 years, the youngest being 24 and the oldest 53 years, in contrast to the average age of 48 of women with clinical gross cervical cancer. Pund et al.[13] found the average age of his in situ group to be 36.6 years. Further evidence of the possible long duration of the noninvasive lesions is offered by Knight, who reported a case in which a preinvasive lesion was found in an amputated cervix. The neoplasm was found to be still present in the remainder of the cervix five years later.

Whether all carcinomas in situ are destined to develop into clinical carcinoma cannot be stated. It is probable that many women harboring the condition die of other causes before the lesion develops to the stage where it becomes clinically apparent. However, the microscopic and clinical evidence is such that it is our belief that they should not be considered "precancerous" lesions but rather an early stage of true cancer.

From the standpoint of reducing the mortality from cervical cancer, this lesion assumes great proportions. Here is a lesion, virtually on the surface of the body, detectable by biopsy, which in many instances gives us years of warn-

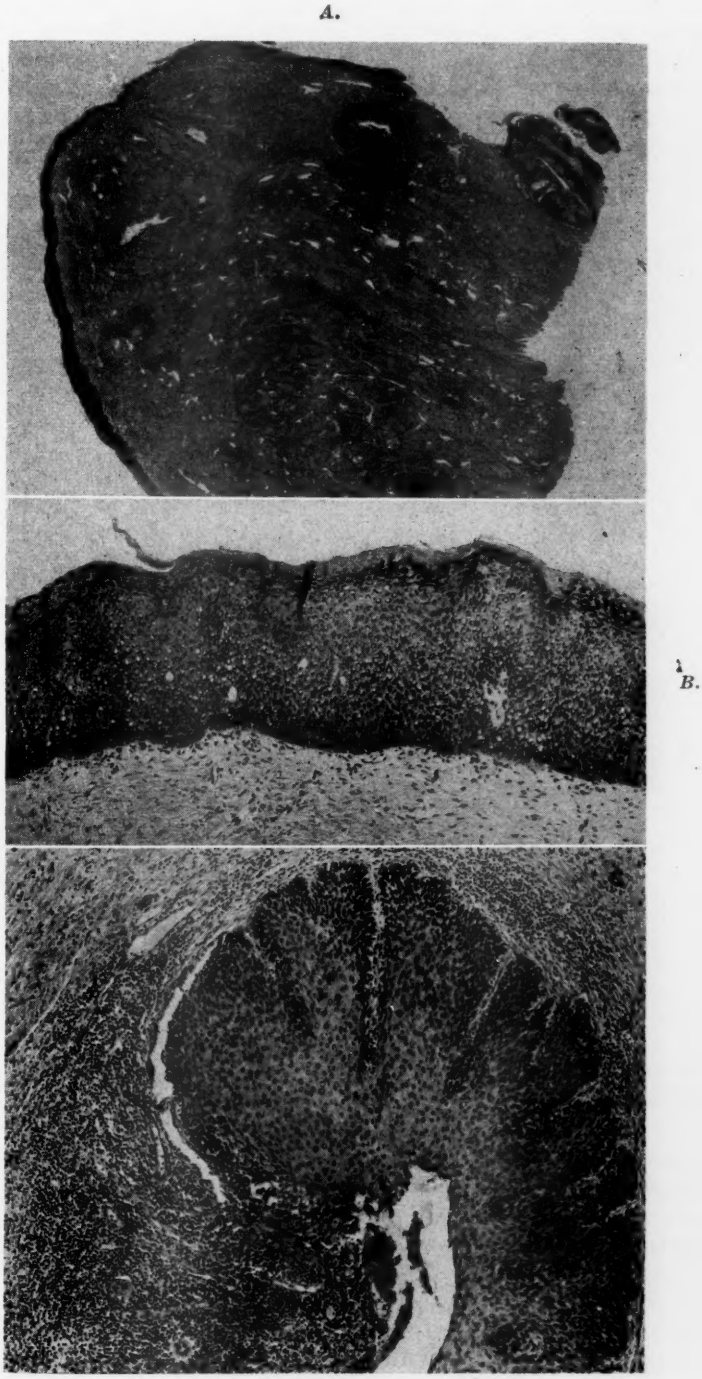


Fig. 11.—Path. No. 54078. *A*. Low power of entire cervical lip, showing extensive carcinoma in situ and areas of invasive cancer. *B*. High power of surface epithelium. *C*. High power of invasive area.

ing before it becomes a lethal lesion. In at least seven of the cases which eventually showed invasive cancer, the cervix appeared normal in all respects and the biopsies were made purely routinely in our study of cervices in women who were to have hysterectomies for benign lesions, such as myomata. In none of the patients of this series did the cervix present the clinical picture of cancer. The majority, however, did present some abnormal appearance and were diagnosed clinically as cervicitis, erosion, eversion, laceration, and leucoplakia. Since we have found almost all of these early lesions arising in the stratified squamous

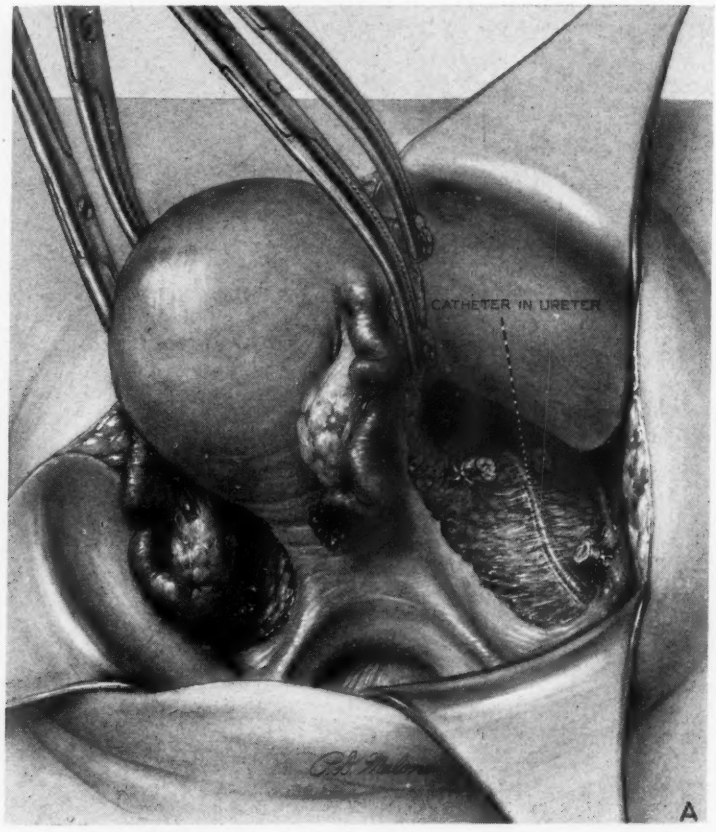


Fig. 12, *A-D.*—Modified Wertheim operation.

A. Broad ligament has been opened widely, exposing ureter which has been catheterized. Uterine vessels have been ligated at some distance from the uterus.

epithelium at its junction with the columnar epithelium, we have a guide as to where to take our biopsies when no local lesion is visible. The sharp demarcation between the pink squamous epithelium and the deep red columnar epithelial surface is usually clearly visible. Occasionally this junction is within the cervical canal, a point not to be forgotten in taking biopsy specimens.

With the use of the ordinary punch biopsy forceps, troublesome bleeding is rare. Recently, we have routinely inserted a Tampax after taking the biopsy and instructed the patient to withdraw it on the following day. Occasionally we have touched the biopsy site with the cautery to stop an active ooze.

We are omitting any comments concerning the diagnosis of carcinoma in situ by cytologic methods. At the present time we do not have sufficient data on this phase to justify any conclusions and we know of no other workers who have enough data to be significant.

From the standpoint of symptomatology, little is to be said concerning this group of cases except to emphasize that often these lesions are completely asymptomatic; but of equal importance is the fact that 58 per cent of these women had some type of irregular vaginal bleeding. Of these, however, this symptom was the presenting complaint in only a few. In the majority it was elicited only through a careful and complete investigation of the history. We were impressed with the fact that in many of the cases in which abnormal bleeding was present it took the form of postcoital spotting. The majority of these lesions were discovered by routine investigation of patients who presented themselves with common gynecologic complaints such as leucorrhea, backache, sterility, dysmenorrhea, and abdominal pain.

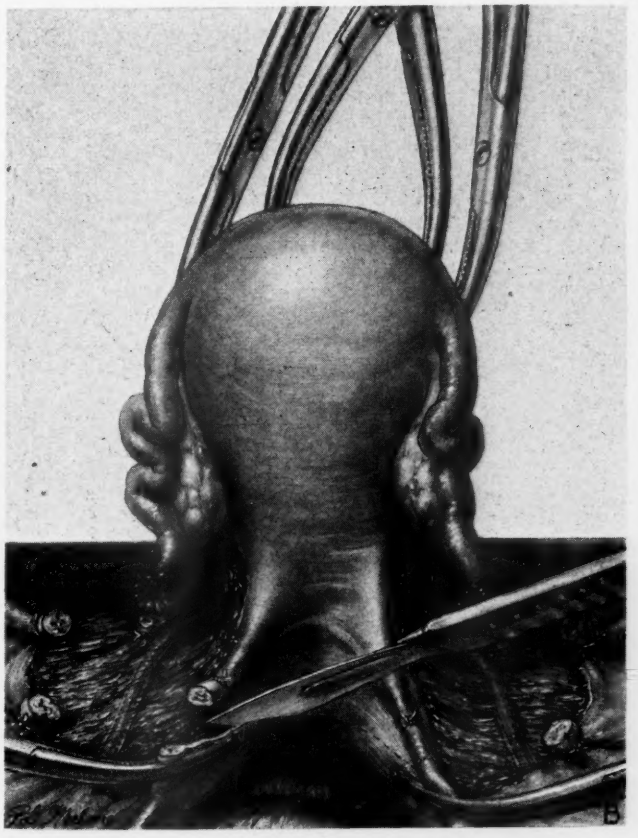


Fig. 12, *B*.—Uterosacral ligaments severed.

The question of the treatment of carcinoma of the cervix, after having been settled for many years in favor of irradiation, has been opened again by the clinical experiments which are at present being undertaken with the Wertheim operation on selected cases falling into Stage I and early Stage II (League of Nations). It is not the purpose of this paper to enter the controversy concerning surgery versus irradiation in the treatment of gross cervical cancer. It is our belief that the above-described microscopic lesions should be considered in a special category from the standpoint of therapy. We regard them as a subgroup of Stage I and the results of their treatment should be reported separately to avoid confusion with existing reports on Stage I.

We originally operated on these patients with the purpose of obtaining the entire cervix for microscopic study. From a study of these cervices it is obvious that one cannot be confident of a cure from cervical amputation. We have three cases in our series in which plugs of carcinomatous tissue were found well up in the cervical canal. The operation which we have performed 67 times is a modification of the Wertheim procedure (Fig. 12). The gland dissection is omitted, but the parametrium is removed for about two cm. on each side of the cervix. A fairly wide cuff of the vagina is removed with the cervix because we have frequently observed a widespread involvement of the surface by the intraepithelial growth, even when its appearance was normal. The pubocervical fascia is not stripped from the vagina as is our custom in performing total hysterectomy for benign disease (Fig. 12, *C*).

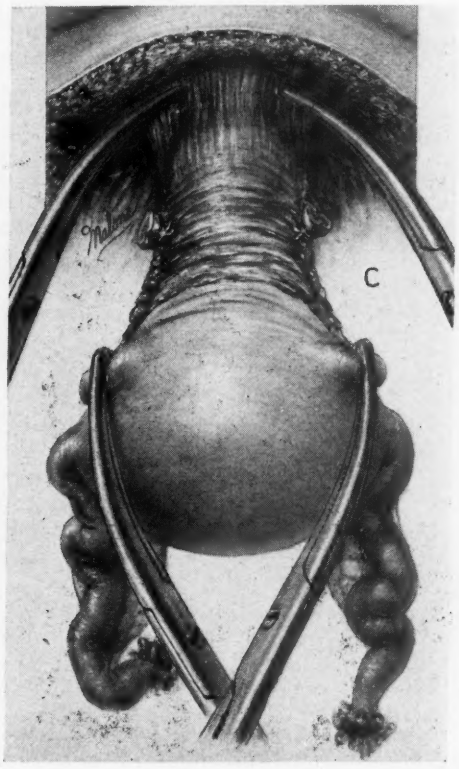


Fig. 12, *C*.—Pubovesico-cervical fascia is left attached to vagina and clamped with it before amputation.

Preoperative ureteral catheterization is a great convenience and safeguard. It is recognized that the ureters can usually be isolated readily without catheterization but at times considerable dissection is necessary, particularly on fat individuals. Bleeding may ensue and stripping the ureter of its blood supply may result in fistula. With catheters in the ureters, the operator can travel down the parametrial regions rapidly and safely by simply palpating the catheter before placing each clamp. We have had no ureteral fistulas in our series. The vagina may be closed or drained, depending on the preference of the operator (Fig. 12, *D*). We have observed no advantage in drainage.

Since many of these lesions occur in young women and since the ovary is a place of late metastasis of cervical cancer, we have saved an ovary in some of the younger women. The theoretical objection to this might be advanced on the basis of preservation of the source of estrogen in the presence of malignancy. Although estrogen is the growth hormone of the sex organs, there is no real clinical evidence to indicate that it is a factor in the production of cervical cancer. Our results have vindicated our decision to obviate bilateral oophorectomy in the younger women. Our results to date also justify our decision to forego lymphadenectomy in these microscopic lesions.

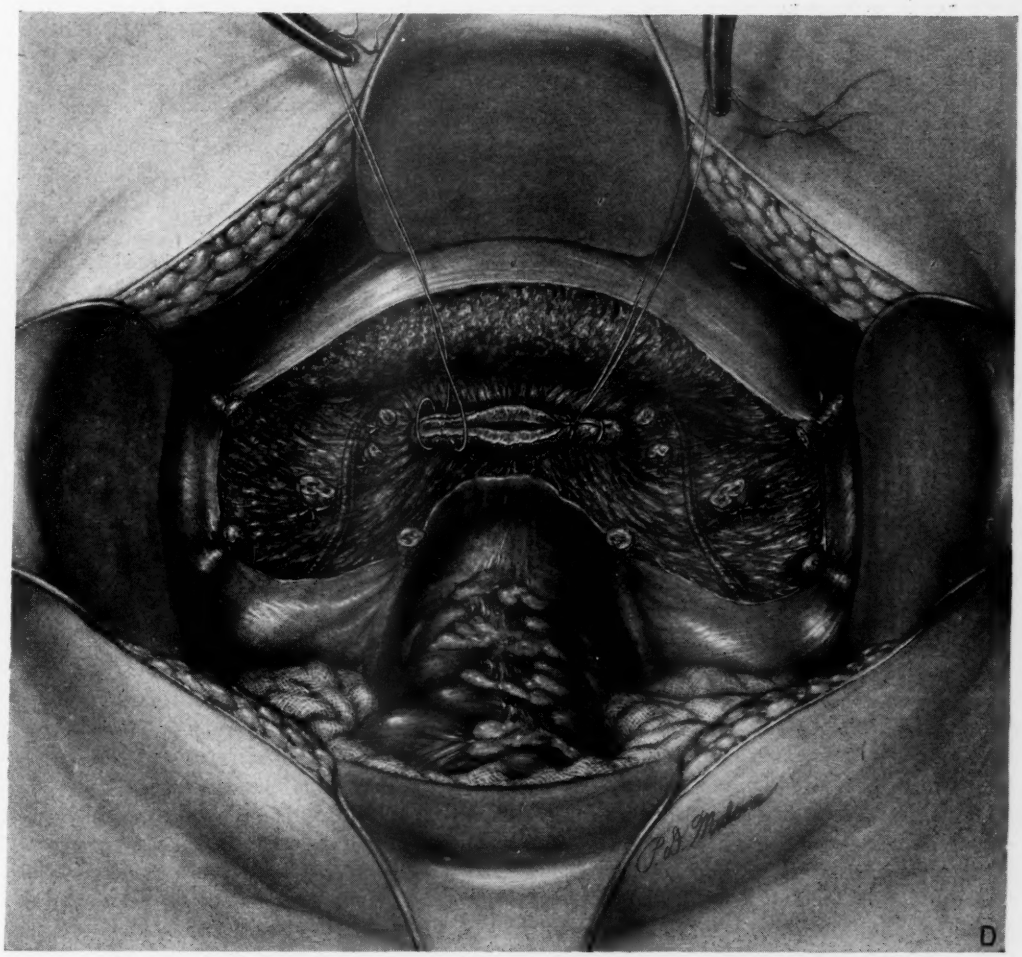


Fig. 12, *D*.—Vagina being closed before its suspension and peritonealization.

All of our 67 cases operated upon between Jan. 1, 1940, and Jan. 1, 1948, are living and without recurrence. Although we realize that sufficient time has not elapsed to attach much statistical significance to these results, we are much encouraged by them and have seen no reason to change our therapeutic attack. Our only death occurred in one of the seven cases in which irradiation therapy was used.

Finally, we wish to emphasize that this study has no bearing upon the present-day controversy of the Wertheim operation versus irradiation in gross cervical cancer. We regard these cases as a special group and we have treated them in a special manner. We would, indeed, be greatly distressed to have the above results used in support of the operative treatment of gross cervical carcinoma. It would be particularly regrettable if the impression were obtained that gross cervical cancer should be treated by an operation in which gland dissection is omitted.

The authors wish to express their appreciation to Miss Eva Hildebrandt, chief tissue technician, for her great industry in cutting thousands of sections, without which this study could not have been made.

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Discussion

DR. LEWIS C. SCHEFFEY, Philadelphia, Pa.—Once more Dr. TeLinde, with the able cooperation of Dr. Galvin and their associated workers, has presented further evidence of continued and meticulous histologic and clinical observation concerning noninvasive cervical carcinoma in which actual invasion was discovered subsequently.

This present action clarifies to a fine degree the criteria set forth with regard to the diagnosis of carcinoma in situ. It is one thing, however, to declare these criteria and another to interpret them properly. What to one pathologist might appear to be a variation in cellular structure and sufficient to be called carcinoma, might to another represent only hyperplasia. This is not true of the author's report, for they have shown how one must be extremely careful not to confuse a tangential section with a focal proliferation of the cells, a difficulty that may be encountered by even the most experienced tissue worker.

As is the case with the skin, the bronchus, and elsewhere, it is probably true that carcinoma begins in the basal cells. Whether or not basal-cell hyperactivity is always a precursor of carcinoma is controversial, as the authors have been frank to admit. Regardless of this conflict of opinion, however, there seems to be little doubt of the author's correct viewpoint on the existence of intraepithelial cancer as revealed by these very complete studies and follow-up observations on 75 patients with cervical carcinoma in situ seen since 1940. In fact, I would now go a step further than they and refer to such lesions simply as "carcinoma" rather than speak of them as "an early stage of true cancer"—and this implies implicit confidence in their research.

It is desirable to emphasize again that a long interval of time may elapse between recognition of carcinoma in situ and the development of a truly invasive lesion, for such occurrences are sometimes observed in carcinoma elsewhere, as for instance on the face. The authors have cited references to such instances but an explanation of these vagaries is still to be found. In this connection I would like to place on record the case of a patient whose cervical tissue in 1924 showed what we would now consider carcinoma in situ, but in whom no further treatment was instituted at that time because of laxity in truly evaluating the

abnormality. Nine years later, in 1933, without interval observation, the patient appeared with a Stage III carcinomatous lesion of the cervix. This somewhat parallels the case of Stevenson and Scipiades cited by the authors.

At Jefferson Hospital we have been endeavoring to carry out a study of this character, but to date have no comparable series to report upon. To some extent this has been due to the conservative attitude previously taken by us with respect to demanding actual invasion as the criteria of malignancy. We do have at present, however, six patients under observation for several years in whom primary cervical biopsy could be considered as representing carcinoma in situ, and in all of whom subsequent endocervical resections of some magnitude revealed nothing even to suggest further existence of an intraepithelial lesion. This might be interpreted as indicating elimination of the cancer by the initial biopsy, but, in any event, no further treatment has been given these patients—and this for the sole purpose of trying to learn more about the situation by simply observing these patients at regular intervals for a continuing long period of time.

For the past year or more we have chosen to deal with any cervix showing abnormality, whether local symptoms are present or not, by a circular scalpel biopsy to include the squamous-columnar line of demarcation, following this by endothermic resection using the loop. We prefer this technique to punch or multiple biopsy methods. Certainly the pathologist prefers ample, uncharred sections of tissue. To date, in several hundred routine cervices serially studied in this manner, no carcinoma in situ has been reported.

The authors have purposely omitted reference to the diagnosis of carcinoma by cytologic methods. It might interest them to know that in the cancer detection clinics of Philadelphia, conducted under the auspices of the Donner Foundation in conjunction with the Philadelphia County Medical Society, my departmental associate, Dr. A. E. Rakoff, has studied 5,000 vaginal smears cytologically. Of six positive smears found, only one was from a patient in whom the signs and symptoms did not actually suggest cervical carcinoma. This is important from the point of view of a screening program, for a single negative report means only that. On the other hand, the Boston group (Hertig, Fremont-Smith, Graham and Meigs) have reported a relatively high number of positive smears in preinvasive carcinoma that compare to better advantage than initial biopsy in one series mentioned.

One word as to treatment. It would appear that, if we accept the concept of malignancy without reservation, then therapy should be in full measure, whether by irradiation or by surgery. The authors, however, have shown in their follow-up that their method of surgical management has to date been adequate with respect to survival.

DR. ROBERT L. FAULKNER, Cleveland, Ohio.—The epithelial changes characteristic of noninvasive carcinoma, or carcinoma in situ, have been recognized and talked about by dermatologists for many years. As is well known, they are seen in such skin conditions as Bowen's dermatosis, senile and arsenic keratoses, and in leucoplakia.

Extensive study of such changes in the epithelium of the cervix uteri, in which the author of this paper has taken an active part for a long time, is of more recent date. Previously, these lesions were thought to be exceedingly rare in any mucous membrane surface epithelium.

His emphasis, now, through additional experience, on activity, or proliferation of cells in the basal layer of the epithelium puts us a step closer in cervical histopathology to the dermatologist and his experience with basal-cell carcinoma—a lesion usually of sluggish growth and benign nature, but which may become dangerous at any time.

Quite properly the author points out that whatever their form, these epithelial changes occur commonly at or near the margin of invasive carcinoma and very rarely as solitary isolated alterations. Such a fact makes debatable the method of treatment. Isolated epithelial lesions of this type are undoubtedly cured by conization or amputation of the cervix, but who has the courage to stop there when it is never known what the remainder of the cervix may contain?

The logical danger to be seen in Dr. TeLinde's handling of these patients is that his treatment is also less than adequate surgical treatment for actual carcinoma of the cervix,

though quite adequate probably for 20 of his 75 patients. The remainder of his patients have small, but not necessarily early, carcinomas and before any opinion is formed whatsoever, we must await his report of five-year survivals.

As a general teaching concept, it would seem that emphasis on carcinoma in situ with conservative operation has stirred up interest in the study of cervical epithelium, but it has also contributed to the present furor for return to surgical treatment of carcinoma of the cervix in an unhealthy manner. In the first place, the mere mention of "carcinoma in situ" is beginning to provide in some quarters an excuse for operation—whether such a lesion actually exists, as it does rarely, or turns out to be, as is more common, the margin of an invasive cancer. Psychologically, with a laboratory report of carcinoma in situ, the pathologist is *allowed* to share the responsibility for later treatment failure. It is human nature, too, to welcome the return of an operation which anybody can perform, but which admittedly is inadequate for cure of cancer. It would seem that in this combination of circumstances may eventually lie elements of trouble and danger, if acceptance becomes widespread.

DR. THOMAS C. PEIGHTAL, New York City.—Since 1944, when Dr. TeLinde reported that 15 out of 16 carcinomas in situ also showed evidence of invasion, he has now collected a total of 75 cases in which this diagnosis of intraepithelial cancer has been histologically identified from biopsies.

During the collection of this data he has been impressed with the importance of basal-cell hyperactivity which has been seen to occur alone, in conjunction with carcinoma in situ, and surrounding frank invasive cancer of the cervix. He asks us to help him answer three questions concerning basal-cell hyperactivity, most pertinent of which is, "Does basal-cell hyperactivity precede carcinoma in situ?" Or, to put it another way, "Is basal-cell hyperactivity just a pathologic step earlier than intraepithelial cancer?

Leucoplakia, so-called, may proceed to a degenerative benign type of lesion, or it may undergo basal-cell hyperactivity, often with keratinization of the upper layers. Basal-cell hyperactivity is often seen in the same section with carcinoma in situ.

It is only through such reports as Dr. TeLinde's, which may come from many other clinics, that this important question can be answered. We feel that basal-cell hyperactivity in biopsy material is a grave warning—not to be regarded lightly—and that its presence calls for repeated biopsy at frequent intervals. We agree with Dr. TeLinde that this basal-cell hyperactivity had best be considered as precancerous until proved otherwise.

As regards carcinoma in situ, Dr. TeLinde has shown that 73.3 per cent of his cases had, at the time of biopsy, frank invasive cancer within the cervix (55 out of 75 cases). For this reason we agree too that carcinoma in situ is no longer to be regarded as merely precancerous but as true cancer and, therefore, in all instances, must be treated as if it were frank invasive cancer.

We use the Schiller test as an aid in obtaining biopsies and emphasize that the examiner must be alert to the slighest abnormal epithelial changes. The historian too must be careful in eliciting symptoms for, as Dr. TeLinde states, "While many of these women are asymptomatic," at least 58 per cent of his cases had some type of irregular bleeding—most often postcoital spotting.

Dr. TeLinde lists 17 cases of carcinoma in situ from other sources which ultimately went on to invasive cancer in from three to nine years. To this list we would add another case.

Dr. TeLinde, where possible, treated his cases by modified Wertheim procedure (67 of the 75 cases were so treated), in no instances removed the retroperitoneal lymph nodes, and in a few young women even left in the ovaries.

This is the only part of his paper to which we cannot wholeheartedly agree. In the first place, we feel one cannot know how often nodes may be involved even in carcinoma in situ cases unless one dissects out these nodes in a goodly number of cases. Again, since 73 per cent of his carcinoma in situ cases really had invasive cancer, it is more than likely that some of these women had positive nodes already at the time of his modified Wertheim procedure. We shall be interested to know what his follow-up on these 67 cases will show in the next few years. Either his omission of node dissection will be justified or his percentage

of recurrence will make him remove the nodes in the future. Time will tell but we urge that in a sufficient number of instances node dissection be carried out to establish the incidence of their involvement in these early lesions.

Dr. TeLinde quotes Schiller as reporting at least three recurrences in five years or less after hysterectomy in such cases.

We would emphasize that trachelectomy alone as a treatment for carcinoma in situ is definitely inadequate. Time alone will tell whether he is justified in preserving ovaries in the younger women.

There are some among us who, I am sure, will not agree that surgery is the best method of treatment for these early cases; and will maintain that this is one group at least in which radium and x-ray may well produce their best results. As Dr. TeLinde pointed out, "This study has no bearing on the present-day controversy of the Wertheim operation versus irradiation in gross cervical cancer. This is a special group which should be treated by surgery if you like, by radium if you prefer that method; but let us keep them segregated and in reporting the results through the years let time alone assess our efforts."

Dr. TeLinde's work has greatly increased the sum total of our knowledge concerning precancerous and early cancerous changes in the cervical epithelium. He has given us the stimulus to be on the lookout for these changes, has taught us how to identify them, and how best to treat them. He, more than anyone else, has kept our specialty abreast clinically and pathologically with the trend of the times—namely, early cancer detection—and has given us the ability to evaluate competently the cervical epithelial changes in the increasing multitude of women that our national cancer drive is daily sending to us for examination.

DR. E. D. PLASS, Iowa City, Iowa.—Some work my colleagues, O. F. Kraushaar, J. T. Bradbury, and W. E. Brown, have done in the past two years seems pertinent to this discussion. Using the Papanicolaou method, they have screened 5,314 women for genital cancer. Among the group of "positive" smears obtained were 14 from women who gave no histories of pelvic abnormalities, and in whom careful digital and visual examinations of the genital tract provided no suspicion of a malignant lesion. Biopsies taken on the basis of the "positive" cytologic abnormalities showed definite evidence of cancer, in five instances the lesion was definitely invasive but in the other nine the diagnosis of "carcinoma in situ" was made with the knowledge that more sections might well have revealed invasion.

Illustrative cases include B. P., aged 64 years, who was treated in the medical department in 1946 for diabetes mellitus. In May, 1947, after admission for a medical check-up, pelvic examination was negative. In December, 1947, diarrhea led to another admission. Pelvic examination was again negative, but the routine vaginal smear showed abnormal cells. Biopsy revealed early invasive carcinoma of the cervix. Treatment was with 4,950 mg. hr. of radium.

G. H., aged 58 years, had had a subtotal hysterectomy in 1934. Five years later, posterior gastroenterostomy was done for duodenal ulcer with pyloric stenosis. On this admission, pyelonephritis with possible uremia was also diagnosed. In 1943, jejunojejunostomy was performed for subacute obstruction. In March, 1948, she was admitted with pyelonephritis. Routine vaginal smear was "positive." Pelvic examination showed an "atrophic cervix." The patient died in uremia and the cervix was obtained at necropsy. Serial sections revealed a "carcinoma in situ."

L. B., aged 30 years, was admitted in March, 1948, because of mild cystitis and trigonitis. Routine vaginal smear showed abnormal cells. Pelvic examination was negative. Cervical biopsy revealed "carcinoma in situ." Total hysterectomy and right salpingo-oophorectomy were done. No neoplasm could be found in the remaining cervical tissue.

On the basis of this work, the thesis is submitted that routine vaginal smears offer the best means of directing further search for very early invasive cervical cancer and "carcinoma in situ."

DR. WILLIAM E. STUDDIFORD, New York City.—Seven of these cases have been discovered at the Bellevue Hospital during the past year, the main method of detection being

cervical biopsy. We have been assisted by cervical cell smears. With one exception they have not offered any particular problem as to treatment. In two cases, the patients had three or four children. In two, the lesion was present in a cervical stump, while two others had complicating fibroids. One patient, aged 27 years, came to the clinic complaining of sterility, with no other symptom.

DR. WILLIAM F. MENGERT, Dallas, Texas.—Since last September, we have done vaginal smears according to the method of Ayre on some 800 women and have found seven with intra-epithelial carcinoma. Not one of these seven women had either sign or symptom of carcinoma. They were simply routine admissions to our out patient clinic. In each instance, of course, smears were followed by biopsies before subsequent operation was performed. In no instance was any definitive treatment done on the basis of the smear alone. We are using the method of scraping with a spatula and believe that is of value since with an intact epithelium cells may not be recovered by aspiration methods. In one instance, scraping of the cervix revealed the presence of neoplastic cells. In order to localize the lesion, the cervix was then divided into four quadrants and four smears made. Two of them, adjacent of course, showed neoplastic cells; the other two did not. Biopsies were made between those two and the carcinoma discovered.

We are beginning to have some evidence that the origin of carcinoma is at the squamous junction of the lateral margins of the cervix, rather than anterior or posterior.

Finally, though Dr. TeLinde needs no further commendation, in our small way everything he said we have found to be entirely correct. Also, I should like to express agreement with Dr. Scheffey that the clinical manifestations are a very short period in the total life cycle of a carcinoma.

DR. JOE V. MEIGS, Boston, Mass.—There is one important thing that has not been mentioned and that is the work of Dr. Harry M. S. Green of Yale University. Apparently cancer is of two types: autonomous, and a type of cancer that progresses through the lymph channels to lymph nodes. If a patient has autonomous cancer, that patient will die. That has been demonstrated in cancer of the breast. We are now attempting to repeat this work in cervical cancer at our hospital. We have had no success as yet but that is one of the investigations we are carrying on.

I think the work of Dr. TeLinde in attempting to pick up early preinvasive cancer is of very great significance because if it can be found early it is possible that we can get it before it has shown any invasion into the lymphatics. The chances of cure would be greater than if it had made progress and reached the lymphatics or if it had become invasive or perhaps autonomous.

DR. TELINDE (Closing).—In regard to the treatment, I want again to emphasize that this operation which falls short of the Wertheim operation is done only in these cases of microscopic cancer. If the lesion is big enough to be seen with the naked eye, we irradiate. We chose surgery in this study to get the cervices for study, to try to decide the question of invasion, and have cut many blocks to do so. The second reason is that in many of the young people, in the twenties, we feel justified in taking the chance of saving an ovary. We have no reason to change our line of treatment at present, but I emphasize that not enough time has elapsed to make our statistics of value to date.

Replying to Dr. Studdiford as to what I would do with that very extensive case, I would say that if a wide cuff of the mucosa was obtained, we would do nothing further. The only cases where we irradiate are those in which we find a rather extensive invasion; in other words, where we have misjudged it clinically. They are not included in our present series.

In regard to cytology, we have had much more experience with biopsy than we have with cytology. One's opinion of the two methods will depend upon the statistics read. In Dr. Meigs' surveys, a larger percentage of cases was found with cytology than with biopsy; at the Memorial Hospital, a higher percentage has been found with biopsy. This is true with us, also, but there is no question that a higher percentage will be found by using both methods, biopsy and cytology, than by using either one method alone.

ADENOCARCINOMA OF THE CERVIX AND OF THE CERVICAL STUMP*†

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THERE were registered in our clinic during the ten years, 1938 to 1947, 1,441 patients with carcinomas of the cervices or of the cervical stumps. Of this number 50 (3.4 per cent) had adenocarcinomas of the cervices or of the cervical stumps. (Table I.) Thirty-one other case records, in which the diagnosis of adenocarcinoma of the cervix or of the cervical stump had been listed, were excluded from this report because a careful review of the records and pathology failed to substantiate with conviction the diagnosis of adenocarcinoma. These thirty-one records were reclassified as squamous-celled carcinoma of the cervix or of the cervical stump.

TABLE I. INCIDENCE OF ADENOCARCINOMA OF THE CERVIX (1938-1947)

YEAR	CERVICAL ADENOCARCINOMA	TOTAL CERVICAL CARCINOMA
1938	4	131
1939	1	137
1940	6	142
1941	7	124
1942	4	156
1943	5	162
1944	3	145
1945	7	157
1946	5	146
1947	8	141
10 years (Total)	50 (3.4%)	1441 (100%)

In the 50 patients in this report, 11 (22 per cent) had adenocarcinomas of the cervical stumps (Table V); 39 (78 per cent) had adenocarcinomas of the cervix.

Incidence: Our incidence of adenocarcinoma of the cervix or of the cervical stump is 3.4 per cent.

Norris,[1] in 1936, collected from the literature 9,509 cervical carcinomas in which 542 (5.7 per cent) adenocarcinomas were diagnosed. In this series, the incidence of adenocarcinoma of the cervix was given by Keller[2] as 1.62 per cent; by Pankow[3] as 1.9 per cent; by Healy[4] as 2.7 per cent; by Martzloff[5] as 5.4 per cent and by Bartlett and Smith[6] as 11.7 per cent.

Masson,[7] in his report of 3,273 patients with carcinomas primary in the cervix, listed 2,744 squamous-cell carcinomas and 176 adenocarcinomas. Nilsson,[8] in 1935, reported 80 patients with adenocarcinomas of the cervix. Cham-

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†Aided by a grant from the Research Council of Duke University.

bers,[9] in 1935, reported 728 patients with carcinomas of the cervix in whom 228 had unsuitable classification for reporting. Of the remaining 500 patients, 450 had squamous-celled carcinomas and 50 had adenocarcinomas. Crossen[10] found in 121 carcinomas of the cervix, 108 squamous-celled carcinomas and 13 adenocarcinomas. Diddle and Bennett[11] in their report on cancer of the cervix in Dallas, Texas, in the years 1936 to 1946, had records of 992 patients in whom cervical carcinomas were diagnosed; 932 were diagnosed as squamous-celled carcinomas and 60 as adenocarcinomas. Simpson et al.,[12] in 1942, found in their institution that there was one adenocarcinoma for every 26 squamous-celled carcinomas and reported 63 adenocarcinomas of the cervix. Numerous other reports may be found in the literature.

Age.—The youngest patient in our series was 27, the oldest 77 years of age. Between the ages of 20 and 40 years, there were 19 patients; between 40 and 70 years, there were 30 patients. Waters[13] reported adenocarcinoma of the cervix in a girl of 7 months. Pollack and Taylor[14] reviewed the literature for carcinoma of the cervix in women 20 years of age or younger, and found 30 patients. Of these 30 patients, 22 had adenocarcinomas of their cervices and the authors added a patient, aged 18 years, who had adenocarcinoma of the cervix. In general, our age grouping follows the groupings reported in the literature but our youngest patient was 27 years of age. General data are also given in Table II.

TABLE II. ADENOCARCINOMA OF THE CERVIX OR OF THE CERVICAL STUMP

AGE	NO.	MARITAL STATUS		RACE		PARITY	
20-30	5	Married	37	White	36	Nulliparous	15
30-40	14	Single	6	Indian	1		
40-50	14	Widowed	4	Negro	13	Multiparous	35
50-60	10	Divorced	3				
60-70	6						
70-77	1						
Totals	50		50		50		50

CLINICAL STAGES	
I	8
II	19
III	18
IV	5
Total	50

Clinical Stages.—(Table II.) The League of Nations Classification was used in expressing the clinical stages of the carcinomas. When the clinical stage was questionable, as, for example, Stage I or Stage II, the former was used. The relationship of the clinical stages to the problems of interpretation of the pathology and to those problems of treatment and ultimate salvage will be discussed in the brief section on pathology.

TABLE III. DURATION OF SYMPTOMS (PATIENT'S RESPONSIBILITY), DELAY IN TREATMENT (DOCTOR'S RESPONSIBILITY)

DURATION OF SYMPTOMS	
Average	9 months
Longest	24 plus months
Shortest	1 month
DELAY IN DIAGNOSIS AND TREATMENT	
Average	10 months
Longest	24 months
Shortest	1 month

Duration of Symptoms and Delay in Diagnosis and Treatment.—In Table III are shown the data on the duration of symptoms, on the delay in diagnosis, and on the delay in starting treatment. As will be noted, the average duration of symptoms was nine months and the average delay in diagnosis and treatment was ten months. These delays are greater than those reported by Miller[15] in his reports on cervical carcinomas. In Table IV are given the clinical stages of the carcinomas found in the 14 patients with known delays in diagnosis and treatment and also the results in these 14 patients.

TABLE IV. PATIENTS WITH OR WITHOUT DELAY IN DIAGNOSIS AND TREATMENT

	PATIENTS
No Delay in Diagnosis or Treatment	30
Unknown Delay in Diagnosis or Treatment	6
Known Delay	14
Total	50

PATIENTS WITH KNOWN DELAY

Stage I	1
Stage II	4
Stage III	6
Stage IV	3
Total	14

RESULTS

Living	1
Unknown	6
Terminal Stage	5
Dead	2
Total	14

Patients With Previous Supravaginal Hysterectomies.—Table V lists the eleven (22 per cent) patients who had had supravaginal hysterectomies performed elsewhere. The first six (54.4 per cent) of these eleven patients were considered by us to have had carcinomas present in the cervices at the time of the operation.

TABLE V. PATIENTS (11) WITH PREVIOUS SUPRAVAGINAL HYSTERECTOMIES

PATIENT	STAGE	TIME LAPSE FROM OPERATION TO DIAGNOSIS OF MALIGNANCY
M. M.	II-III	3 months
H. W.	II-III	6 months
L. D.	III	6 months
O. B.	II	6 months
L. H.	IV	11 months
M. R.	III	14 months
R. S.	IV	6½ years
A. B.	III	8 years
L. M.	II	20 years
P. H.	III	26 years
M. W.	II	27 years

If either squamous-celled carcinomas or adenocarcinomas are found in cervical stumps within twenty-four months following supravaginal hysterectomies, we have assumed that the carcinomas were present at the time of operations. We realize that this is an arbitrary concept but it does give us some working rule. In view of the attitudes now expressed on "carcinoma in situ" and "preinvasive carcinoma" of the cervix, it is probable that even those patients who develop carcinomas in the stump years after operation, may have had cancer

in the cervix at the time of supravaginal hysterectomy. Certainly, our incidence of squamous-celled carcinomas and adenocarcinomas of the cervical stump strengthens our opinion that panhysterectomies should be performed in preference to supravaginal hysterectomies.

Pathology.—No attempt is made in this report to review the literature concerning the various gradings of adenocarcinomas of cervices. That differentiation is difficult between squamous-celled carcinoma and some grades of adenocarcinoma of the cervix, has been reported many times. In this report, we discarded 31 case records which were filed as adenocarcinomas, but which, on careful review, had to be reclassified as squamous-celled carcinomas.

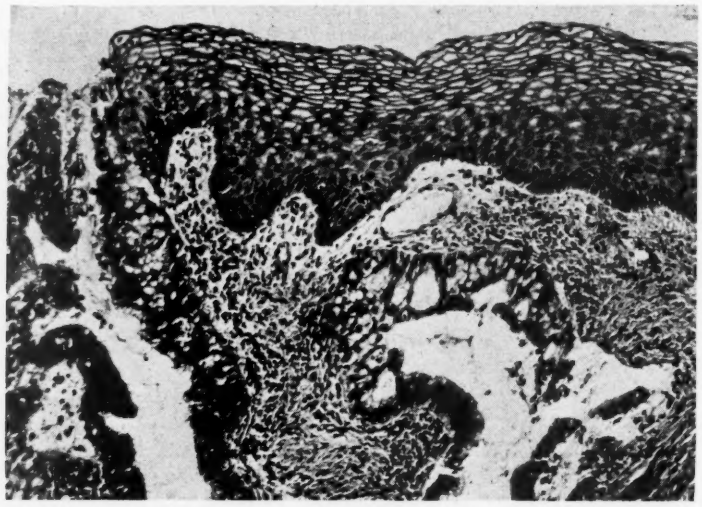

Fig. 1.—Cervical biopsy. Adenocarcinoma of cervix with glandular carcinoma beneath normal squamous epithelium. Low power.

In general, our attempts at grading follow Broders'[16] criteria. The adenomatous growths with good differentiation are listed as Grade I; Grades II and III represent greater degrees of de-differentiation with departure from the normal pattern. Grade IV shows marked degree of anaplasia and unripeness of the cells. As stated by Novak,[17] the personal equation which may enter into the classification in Stages II and III "carries with it no special clinical hazard." His discussion summarizes our attitude in the grading of these adenocarcinomas.

Norris[1] has reviewed the early literature on the various classifications proposed and on the question of the radio-sensitivity or nonradio-sensitivity of adenocarcinoma. Ward[18] and Healy[19] do not consider adenocarcinoma more radio-resistant than squamous-celled carcinoma.

Warren[19] noted the close correlation between the histologic grades of carcinomas and the distribution of metastases. He stressed, however, that the histologic grading was of little value in determining the individual prognosis. The histologic grading was of value in determining radio-sensitivity of the neoplasm and in determining whether the neoplasm was likely to cause metastases. He stated that, as a rule, the more rapidly growing, more anaplastic, and more malignant tumors were sensitive to radio therapy and, therefore, cure of the local growth was common. However, their ability to cause early and wide metastases and infiltrations made them unsatisfactory tumors to treat with radium or other treatments. In his review of the autopsy protocols of 132 pa-

tients who had carcinomas of the cervices, 11 had adenocarcinomas. No metastases were found in one, the regional nodes were involved in six, the distant nodes were involved in six and the lungs and liver were involved in two.

Behney,[20] in his report on 166 autopsies performed on patients with advanced carcinoma of the cervix, also stated that the more anaplastic types of neoplasms were prone to cause more frequent metastases.

Simpson et al.[12] considered the more differentiated neoplasms more radioresistant. Their rate of growth was slow and they tended to remain localized, and, therefore, a higher percentage of cures might be expected. The anaplastic or de-differentiated neoplasms, although more radio-sensitive, showed more rapid growth, wide infiltration, and early metastases with resultant low cure rates.

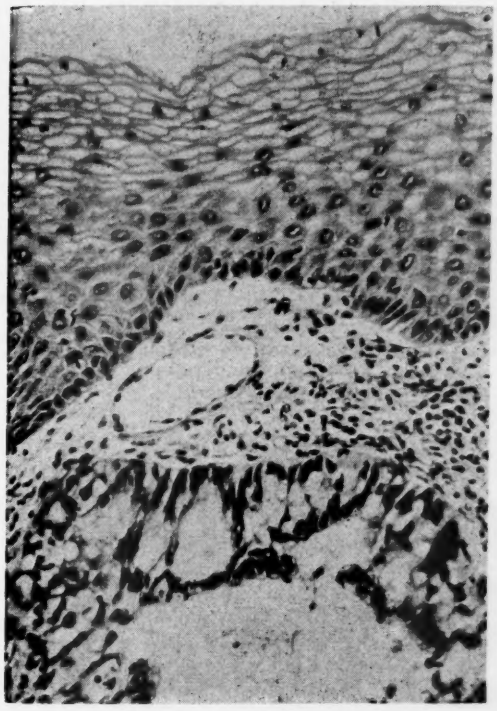

Fig. 2.—Cervical biopsy. Adenocarcinoma of cervix with glandular carcinoma beneath normal squamous epithelium. High power.

We feel that the clinical stage of a neoplasm and the histologic grading are both important in the ultimate salvage.

The number of reports on autopsies done on patients dying with squamous-celled carcinomas and adenocarcinomas of the cervices is strikingly small. Some method should be evolved which would permit the hospitalization of patients in the terminal stages of cancer. The reaction, or lack of reaction, to radiotherapy or operative therapy might be studied thoroughly, intelligently, and carefully.

Martzloff's[21] experience with cervical biopsy material is also instructive. He had the opportunity to compare the biopsy tissue with the tissue removed at hysterectomy in 70 patients with epidermoid carcinoma of the cervix. In one third, the biopsy material was insufficient to make possible a definite classification. We have for years discontinued the use of "biopsy of the cervix" and have substituted "multiple biopsies of the cervix and multiple biopsies of the endocervix."

The use of repeated and repeated Papanicolaou histocytologic smears and of repeated and repeated biopsies of the cervix and endocervix may be the answer to early diagnosis and to correct gradation of the carcinomas.

Papanicolaou smears were done on seven patients in this series of fifty.

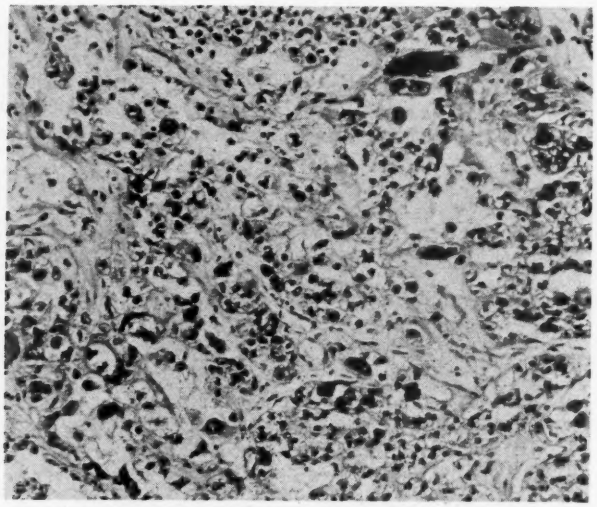

Fig. 3.—Wertheim, cervix. Glandlike structures and anaplastic undifferentiated carcinoma post x-ray and radium.

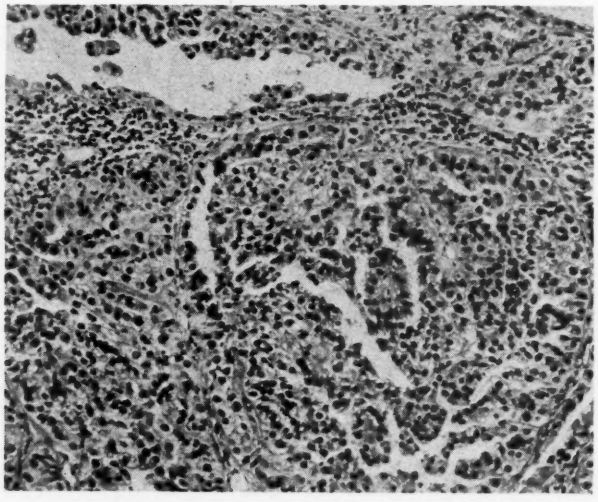

Fig. 4.—Biopsy of cervix. Adenocarcinoma in cervical biopsy after inadequate irradiation over two-year period.

Type V smears were reported in four patients; type IV smears in one patient; type III in two patients. Adenocarcinoma was diagnosed as such in three; as questionable adenocarcinoma in two and as squamous-celled carcinoma in two. With improvement in the histocytologic techniques and with the increasing experience of the workers in these techniques, we believe that routine

"screening" of all women 30 years of age or over who come to our clinic will be useful in detecting possible carcinomas of the uterus at earlier stages than we have seen in the past.

Table VI gives the results of irradiation therapy only. Of 29 patients, only 18 received what we term "adequate" x-ray and radium therapy. Of these 18

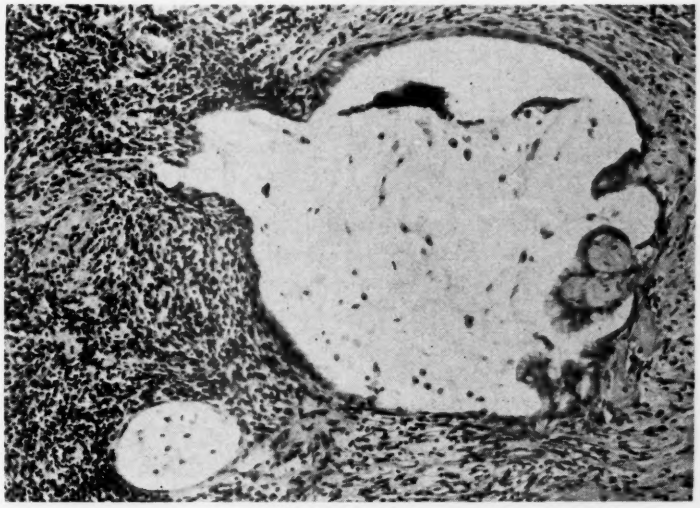

Fig. 5.—Wertheim, lymph node. Mucus-producing glandular pattern. Definitely adenocarcinoma.

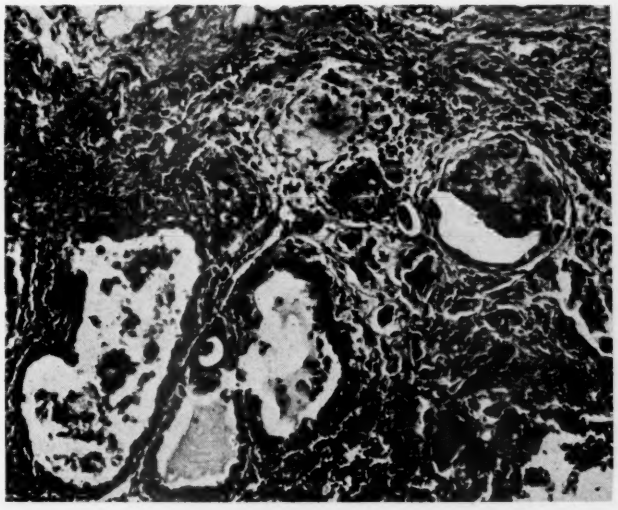

Fig. 6.—Wertheim, lymph node. Metastasis with gland pattern and solid tumor nests.

patients, but two (11.1 per cent) are living, whereas eight are in the terminal stages of cancer. Two are dead of cancer and six are listed as unknown, i.e., presumed to be and counted as dead.

TABLE VI. RESULTS OF IRRADIATION THERAPY ONLY

TREATMENT	NO. OF PATIENTS	RESULTS			
		LIVING	TERMINAL STATE	DEAD	UNKNOWN
Adequate x-ray and radium	18	2	8	2	6
Inadequate x-ray and radium	5	0	4	0	1
Adequate x-ray only	5	0	2	1	2
Adequate radium only	1	0	0	0	1
Totals	29	2	14	3	10

Five patients received "adequate" x-ray therapy only and two are in terminal stages, one is dead of cancer, and two are listed as unknown, i.e., presumed to be and counted as dead.

One patient received adequate radium therapy only and is listed as unknown, i.e., presumed to be and counted as dead.

Five patients received inadequate x-ray and inadequate radium therapy. Four are in the terminal stages and one is listed as unknown, i.e., presumed to be and counted as dead.

The patients are usually responsible for the failures in the attempts to give what we term adequate irradiation therapy. The intelligent patients are cooperative in the matter of permitting careful therapy and good follow-up care. Many of the uninformed patients are remiss in following orders for therapy and follow-up.

TABLE VII. PATIENTS TREATED WITH X-RAY, RADIUM AND OPERATION WITHOUT KNOWN SALVAGE (DEAD, TERMINAL STATE, UNKNOWN)

PT.	STAGE	IRRADIATION THERAPY			OPERATIVE PROCEDURE	PATHOLOGY		RESULTS
		TOTAL R.	VAGINAL CONE	RADIUM MG. HR.		CERVIX	POSITIVE NODES	
H. W.	(Stump) II-III	18,500	3000	3600	Rad. Removal of Stump Radical Lymphaden.	+	L. iliac	Dead
L. M.	(Stump) II	0	0	0		+	0	Terminal
S. R.	I-II	Post-op. 10,600	0	6000	Rad. Hyst. Radical Lymphaden.	0	Bilat. Obt. & Iliacs	Dead
B. G.	III-IV	13,600	3000	0		+	Lt. Obt.	Unknown
M. B.	III	Post-op. 7,450	0	0		Cervix Uterus Vagina	Bilat. Obt. & Iliacs	Terminal
L. F.	IV	0	0	Unknown amt. 17 yrs. prior	Rad. Hyst.	+	Abdo. Carcinoses	Dead
F. B.	III-IV	9,200	500	3800		+	0	Dead
L. F.	I-II	10,500	0	4350		0	0	Unknown
L. D.	(Stump) III-IV	11,100	0	3100	Rad. Removal of Stump.	Cervix Vagina	0	Terminal
N. M.	(Stump) II-III	10,000	0	0		0	0	Dead

Table VII lists those patients treated with x-ray, radium, and operation in whom there was no salvage.

Two patients had radical removals of the cervical stumps and radical pelvic lymphadenectomies. One of these two had adequate preoperative x-ray and radium therapy. The pathology report showed cancer in the cervix and cancer in the left iliac nodes. The patient died later of cancer. The other patient received no x-ray or radium therapy before the radical operation for removal of the stump and the radical pelvic lymphadenectomy. She had cancer in the cervix but no cancer in the nodes. The patient was in the terminal stages of the disease when last seen.

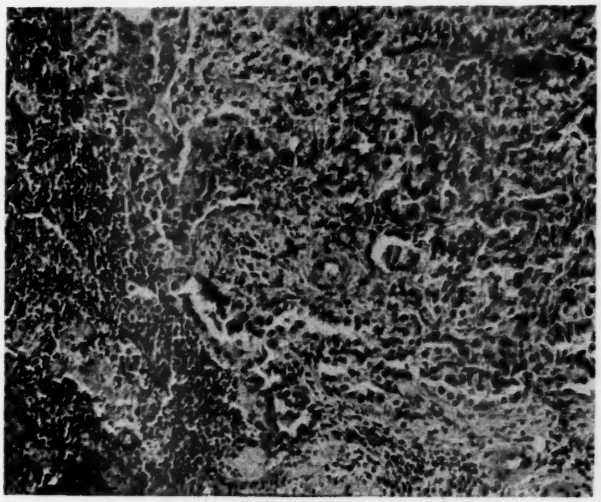

Fig. 7.—Wertheim, lymph node. Metastatic adenocarcinoma to the node; post irradiation.

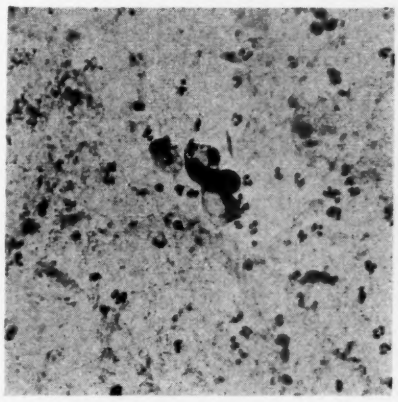

Fig. 8.

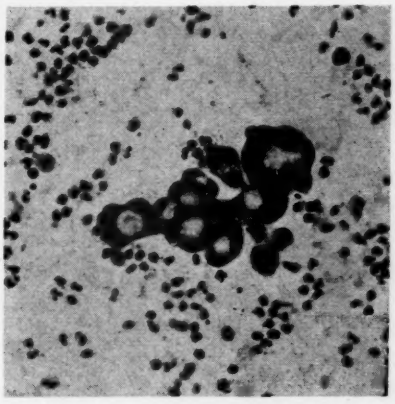

Fig. 9.

Fig. 8.—Papanicolaou smear. Group of vacuolated adenocarcinoma cells.
Fig. 9.—Papanicolaou smears. Single large group of adenocarcinoma cells.

Three patients had radical hysterectomies and radical pelvic lymphadenectomies.

One of these patients had adequate preoperative x-ray therapy only and cancer was found in the cervix and in the left obturator nodes. She is presumed to be dead of cancer. The next patient received adequate preoperative radium therapy only. The cervix showed no cancer but cancer was found bilaterally in the iliac and obturator nodes. She received adequate postoperative x-ray therapy. The patient died later of cancer. The last of these

three patients received no preoperative x-ray or radium. The cervix, the lower uterus, and the vagina showed cancer and cancer was found bilaterally in the iliac and obturator nodes. Adequate postoperative x-ray therapy was given. The patient died later of cancer.

Three patients had radical hysterectomies but did not have radical lymphadenectomies performed. The first patient had received an unknown amount of radium seventeen years before her admission. No preoperative x-ray or radium were given. Operation showed adenocarcinoma of the cervix and of the glands and of the other pelvic structures. She died later of cancer. The second patient received inadequate x-ray and radium therapy preoperatively. Pathology showed adenocarcinoma of the cervix. She died later of cancer. The last patient of these three received adequate x-ray but inadequate radium preoperatively. Pathology showed no cancer in the cervix. She cannot be traced and is presumed to be and is counted as dead.

Two patients had radical removal of the cervical stumps but no radical lymphadenectomies. The first patient received adequate preoperative x-ray and inadequate preoperative radium. Pathology showed carcinoma of the cervix and of the vagina. She is now in the terminal stages of cancer. The second patient received adequate preoperative x-ray therapy but no preoperative radium. The pathology report showed no cancer in the cervical stump. The patient died later of cancer.

Table VIII is the summary of the treatment of the 13 patients who are living.

TABLE VIII. SUMMARY OF TREATMENT IN LIVING PATIENTS (13)

PT.	CLINICAL STAGE	IRRADIATION X-RAY TOTAL R.	CONE	RADIUM MG. HR.	OPERATIVE PROCEDURE	OPERATIVE PATHOLOGY CERVIX	NODES	MONTHS LIVING
M. R.	III	8,604	5040	6000	0	0	0	36
G. C.	II	14,800	3500	6312	0	0	0	96
B. W.	II-III	*8,800	0	0	Radical Hyst.	+	0	14
M. S.	II	13,600	3000	3600		0	0	39
I. C.	II-III	9,600	0	5000		+	0	61
M. W.	cerv. stump II	13,500	3000	0	Rad. Removal of cervical stump	+	0	94
C. S.	I	0	0	0	Rad. Hyst.	+	0	7
A. R.	II	0	0	0	Rad. Lymphad.	+	0	8
A. E.	II	0	0	0		+	0	8
R. M.	I	*10,600	0	0		+	0	24
F. G.	II	7,063	5200	5940		0	Left iliac	60
J. S.	II	13,400	4000	5200		0	0	64
I. W.	I-II	10,300	5200	0		0	0	72

*Postoperative x-ray.

The first two patients had adequate x-ray therapy including adequate x-ray by vaginal cone and adequate radium therapy. No operations were done. The first patient has lived 36 months and the second 96 months.

The third patient had no preoperative x-ray or radium therapy prior to radical hysterectomy and did not have radical pelvic lymphadenectomy. The cervix showed cancer. She received inadequate x-ray therapy postoperatively. The patient is living 14 months following therapy.

The fourth patient had preoperatively adequate x-ray therapy which included 3,000 r. by vaginal cone. She received inadequate preoperative radium. A radical hysterectomy was done. The patient is living 39 months after treatment. The cervix showed no cancer.

The fifth patient had inadequate preoperative x-ray therapy with no vaginal cone therapy and inadequate preoperative radium therapy. A radical hysterectomy was done. The cervix was positive for cancer. She is living 61 months after completion of treatment.

The sixth patient had adenocarcinoma of the cervical stump. She received adequate preoperative x-ray therapy including 3,000 r. by vaginal cone. She had no preoperative radium therapy. She then had radical removal of the cervical stump. The stump showed cancer. She is living 94 months following therapy.

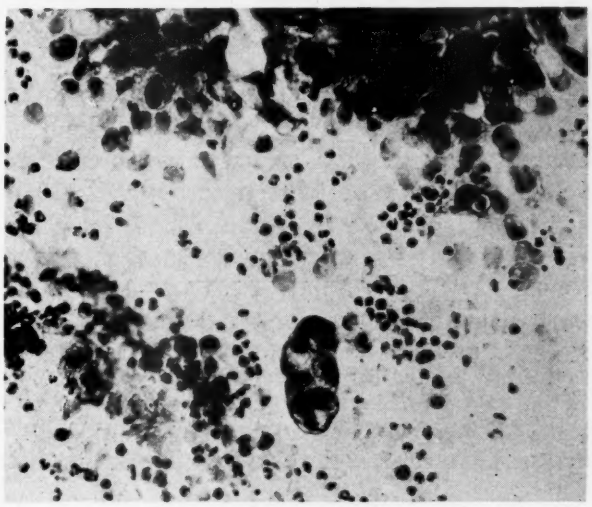

Fig. 10.—Papanicolaou smears. One group of vacuolated adenocarcinoma cells. Edge of large sheet of adenocarcinoma (undifferentiated).

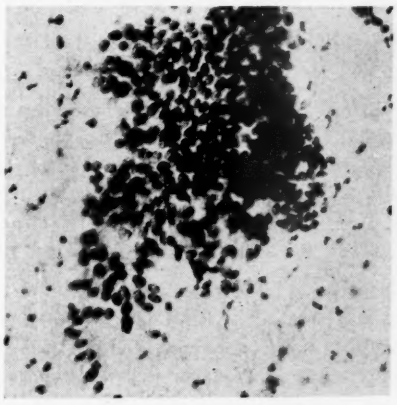

Fig. 11.

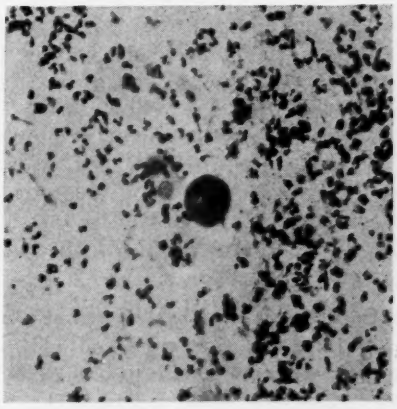

Fig. 12.

Fig. 11.—Papanicolaou smear. Large sheet of small adenocarcinoma cells.
Fig. 12.—Papanicolaou smear. Single clump of adenocarcinoma cells.

The seventh, eighth, and ninth patients had no preoperative x-ray or radium therapy and had radical hysterectomies with radical pelvic lymphadenectomies. The cervices were all positive for cancer, but the nodes showed no cancer. None received postoperative x-ray therapy. The three are living 7, 8, and 8 months, respectively, following therapy.

The tenth patient received no preoperative x-ray or radium therapy and had a radical hysterectomy and radical pelvic lymphadenectomy. The cervix was positive for cancer. No cancer was found in the nodes. She received 10,600 r. of x-ray, postoperatively. She is living 24 months after completion of therapy.

The eleventh, twelfth, and thirteenth patients all received adequate preoperative x-ray therapy, including vaginal cone. Number 11 and Number 12 received preoperatively 5,940 mg. hr. and 5,200 mg. hr. of radium, respectively. Patient 13 received no preoperative radium therapy. Radical hysterectomies and radical pelvic lymphadenectomies were done on all three. The cervices of the three showed no carcinoma. The eleventh patient had carcinoma in the left iliac glands; the twelfth and thirteenth patient had no carcinoma in the glands. They have lived respectively 60, 64, and 72 months.

TABLE IX. RESULTS

CONDITION	NUMBER OF PATIENTS	PER CENT
Living	13	26
Terminal State	18	36
Dead	8	16
Unknown	11	22
Total	50	100

Table IX summarizes the results for the 50 patients. Eight (16 per cent) are known to be dead; eleven (22 per cent) are listed as unknown, i.e., presumed to be and counted as dead. Eighteen (36 per cent) were in the terminal stages of cancer when last seen.

Of the thirteen (26 per cent) patients living at present, only six (12 per cent) have reached or have passed the five-year mark at which we list them as "presumptive" cures.

Complications

There were no deaths due to irradiation or operative treatment.

Pyometra occurred in ten patients and responded to drainage.

Vesicovaginal fistulas occurred once as the result of carcinomatous infiltration and once as the result of operation.

Ureteral strictures were found in two patients and were dilated.

Pyelonephritis occurred in two patients.

Rectovaginal fistulas occurred twice, once as the result of cancer extension and once as a postoperative complication.

Proctitis developed in five patients. Rectal stricture was found in one patient. Thrombophlebitis occurred twice; once postoperatively and once spontaneously. Two patients (G. C. and I. C.) are interesting in that each developed adenocarcinoma of the bladder after treatment for adenocarcinoma of the cervix.

G. C., Stage II, adenocarcinoma of the cervix, was treated in 1940 with 11,300 r. through 2 anterior and 2 posterior ports and 3,500 r. by vaginal cone. She received 6,312 mg. hr. of radium. No operation was done. In 1942, adenocarcinoma of the bladder was diagnosed and the cancer was treated with radium. The patient is now living, eight years after the treatment for adenocarcinoma of the cervix and six years after treatment of the adenocarcinoma of the bladder.

I. C., Stage III, adenocarcinoma of the cervix, was treated in 1943 by 9,600 r. through 2 anterior and 2 posterior ports. No vaginal cone therapy was given. She received 5,000 mg. hr. of radium in 1943. In 1943, she had radical hysterectomy. In 1944, adenocarcinoma of the bladder was diagnosed and was treated with radium. The patient is living and well five years after the radiation therapy and operation for adenocarcinoma of the cervix and vagina and four years after the treatment of the adenocarcinoma of the bladder.

Summary

1. The incidence of adenocarcinoma of the cervix or of the cervical stump was 3.4 per cent in a series of 1,441 patients with carcinomas of the cervices

or of the cervical stumps who were registered in the ten years, 1938 to 1947.

2. Forty-two of the adenocarcinomas, when first seen, were Stage II, III, or IV. Histologic grading was, in all probability, inaccurate but the incidence of undifferentiated carcinomas was high.

3. The average duration of symptoms before the patients were seen was nine months; the average delay in diagnosis and the starting of treatment was ten months.

4. There were eleven (22 per cent) patients in this series of 50 who had adenocarcinomas of the cervical stumps. This incidence, with our high incidence of squamous-celled carcinomas in cervical stumps, strengthens our conviction that panhysterectomies are preferable to supravaginal hysterectomies.

5. "Adequate" x-ray and radium therapy, as the only method of treatment, was given 18 patients. Two (11.1 per cent) are living; one has lived 36 months and one 96 months with no evidence of disease. The other 16 patients are either in the terminal stages of the disease, are dead, or are lost and counted as dead of cancer.

6. Five patients had radical hysterectomies or radical removals of the cervical stumps and radical pelvic lymphadenectomies. Cancer was found in the cervices of four patients, in the uterus and vagina in one, and in the pelvic lymph nodes in four. All of these patients died of cancer.

7. Seven patients had radical hysterectomies and radical pelvic lymphadenectomies. In one the left iliac nodes showed cancer; in the other six there were no positive nodes. This patient with positive nodes has lived 60 months and two other patients have lived 64 and 72 months, respectively, without evidence of cancer. The four other patients have lived 24, 8, 8, and 7 months, respectively, without evidence of cancer.

8. There were no deaths in this series from either irradiation therapy or from operations.

9. Of the thirteen (26 per cent) patients living at present without evidence of disease, only six (12 per cent) have reached or passed the five-year limit at which we list the patients as "presumptive" cures.

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Discussion

DR. KARL MARTZLOFF, Portland, Oregon.—The adenocarcinomas of the cervix which Dr. Carter described, I assume, represent tumors that occur primarily in the cervix or the residual cervical stump after supracervical hysterectomy. Therefore, I would like to emphasize additionally the observation that adenocarcinoma of the cervical stump may on occasion represent remanifestation of an endometrial cancer of the more proximal uterus that has been either overlooked or improperly treated by supracervical hysterectomy.

I agree thoroughly with his observations concerning the difficulties involved in the diagnosis of some specimens of cervical adenocarcinoma when the tumor shows a high degree of differentiation or when aggregations of Gärtner duct tubules showing some deviation from normal provide problems of interpretation. The difficulty here is considerably different from the one encountered in some of the argumentative problems evolving about the epidermoid cancers. In the latter, as was demonstrated this morning by Dr. TeLinde, there is ordinarily no difficulty in deciding that a given zone in superficial stratified epithelium or in the squamous cell metaplasia of a gland represents a neoplastic change.

When differences of opinion occur, the point at issue then generally centers about the decision as to whether the neoplasia represents merely a noninvasive carcinomatoid change or whether actual invasion and established cancer exist.

However, where well-differentiated adenocarcinoma or what are interpreted as altered Gärtner ducts are concerned one's difficulty is immediately apparent, for the perplexing question which confronts one now is, are these glands neoplastic, or is this a picture of bizarre benign proliferation? In some such instances, irrespective of the diagnosis under which a lesion is finally catalogued, the true answer in my experience may be never attained until perchance exploratory operation or death proves the malignant character of a process previously considered as benign.

The foregoing considerations, I believe, explain the profound variations that occur in statistical reports concerning the comparative incidence of adenocarcinomas among cervical cancers. Percentages that vary from 1.6 to 11.7 per cent are far removed from normal statistical variation and error and, therefore, represent fundamental differences in criteria utilized by different individuals for the diagnosis of adenocarcinoma. Dr. Carter's figures admirably demonstrate this point, for among 81 patients who had been catalogued originally as having adenocarcinoma of the cervix, only 50 of those diagnoses withstood the scrutiny of a critical review. Although this discussion does not concern the epidermoid cervical cancers, I believe it is pertinent that a similar critical review by many laboratories for this group of tumors would also reveal little factual support for some of their diagnoses.

The amount and manner of obtaining tissue for biopsy are also inextricably involved in the diagnostic problem. Small pieces of tissue obtained with the endothermy unit by so-called conization are, I believe, an open invitation to error. The heat which causes outright readily recognizable peripheral tissue destruction also permeates the underlying tissue for varying depths and produces here bizarre nuclear changes that are often difficult of interpretation. Likewise the minute tissue fragments obtained with a small biopsy punch, because of their inadequacy, are a source of real concern to many of our pathologists and not infrequently preclude a definitive diagnosis where it might otherwise have been feasible. It is a fair assumption that errors occur at both extremes of the statistical scale and it is doubtful that any board of expert gynecologic pathologists passing judgment on adequately obtained and prepared tissues could wholly eliminate such differences.

Variations in diagnostic accuracy, as a corollary, must then reflect the ultimate rate of cure reported following therapy in such a group of selected patients. I am sure that such diagnostic misinterpretation must play a role in explaining, for example, some of the dis-

crepancies reported concerning the radiation sensitivity or resistance of this particular class of tumors as well as some of the cures reported from the use of comparatively minute doses of radium radiation.

In concluson, I would like to call particular attention to the relatively uncommon mucoid type of cervical adenocarcinoma. This, I believe, is both highly radiation resistant and generally slowly progressive. It should be subjected, I believe, to the radical operation without waiting for postradiation remanifestation as long as it is in an operable stage, namely, League of Nations clinical Stages 1 and 2 or, possibly 3. Remanifestations of these tumors after temporary suppression with intensive radiation therapy may be difficult to recognize because curettage may bring away no recognizable tissue. However, a recurring mucoid vaginal discharge should arouse suspicion which may be confirmed by obtaining with the scalpel a large segment of tissue for biopsy.

DR. GEORGE GRAY WARD, New York City.—At the Woman's Hospital in New York we have been interested in carcinoma of the stump and its treatment.

In 879 carcinoma of the cervix cases seen from 1919 to 1940, 61 were stump cases following a previous hysterectomy or 6.7 per cent; 49 of these were observed for five years after treatment with 21 living, or 42.8 per cent; 20 were observed for ten years, 10 of whom were living, or 50 per cent.

In the same period of five years, our salvage of all carcinoma of the cervix cases was 28.5 per cent.

Thirty-two of these stump cases arose three years after hysterectomy, or 3.6 per cent, which is about the usual average in other clinics. Sixteen were classed as early, and 45 were advanced; 47 were classified as squamous carcinoma, of whom 20 survived five years, or 44 per cent, and 9 survived ten years, or 20 per cent.

Twelve cases were classified as adenocarcinoma, or 2 per cent; two survived five years, or 20 per cent; and only one survived ten years.

In a recent analysis of 236 cases of carcinoma of the cervix originating from 1933 to 1940 observed for five years, there was a relative survival of 35 per cent.

Of these 236 cases, fifteen were stump carcinoma, or 6.4 per cent with a five-year salvage of 46.7 per cent.

The adenocarcinoma cases averaged as in the previous report.

In our opinion, stump cases as a rule do better with radium treatment than cases in which the whole uterus is present. Dr. Scheffey and Dr. Behney have also reported similar results.

DR. CARTER (Closing).—Certainly the main point is early diagnosis. Diagnosis of carcinoma may be made early by taking repeated histocytologic smears and by repeated biopsies of the cervix and endocervix.

The contributions of the Fellows of this Society to the subject of cancer have been real. We will be interested in seeing whether we will be able to show a 25 per cent cure rate in adenocarcinoma of the cervix. In patients who are good operative risks, we feel that there is a place for the radical hysterectomy and the radical pelvic lymphadenectomy. If patients with metastatic cancer in the glands can be proved to be cured by the operative procedure, then the operative procedure should have a place in the treatment.

ADENOCARCINOMA OF THE UTERUS

Observations on Treatment and Histologic Findings Following Intracavitary Radiation

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DUE, in a large measure, to the recent augmented activities of the American Cancer Society, the people of this country are becoming increasingly "cancer conscious." The value of this work is manifested by the popular demand for prophylactic examination for the early detection of malignancy. Already the detection centers are crowded with those requesting investigation and the increasing number of early malignant lesions discovered attests the value of this work. With the existing educational program, women are more cognizant of the meaning of menstrual irregularities and atypical forms of vaginal bleeding in the latter years of life. As is well known, women with menstrual dysfunction at this time are frequently lulled into a false sense of security, believing it to be a normal climacteric event, and refrain from pelvic examination. Today, an increasing number of women come biannually for pelvic and breast examinations and many are realizing that abnormal bleeding, although painless, requires prompt and competent investigation. Early examination for the detection of malignancy is of the essence and is of especial importance in adenocarcinoma of the uterus. In the early stages of this condition the pelvic examination may be entirely negative, minimal bleeding may be the only danger signal and the diagnosis made only by examination of the endometrium. In the past it was not uncommon for the roentgenologist to treat supposed menopausal bleeding with roentgen therapy without first having obtained a definite diagnosis by curettage. However, with increasing knowledge, this dangerous procedure has decreased to a minimum.

Analysis of Clinical Factors

As is well known, the early symptoms of adenocarcinoma may be quite minimal, the only indication of pathology being painless bleeding, either in the form of menorrhagia or metrorrhagia. This symptom may exist for a long period of time and the condition still remain in the realm of operability. Small bleeding associated with normal pelvic findings may be interpreted as a manifestation of the climacteric or occurring during the childbearing age as due to hyperplasia of the endometrium or to some other type of dysfunctional bleeding. Adenocarcinoma of the corpus frequently arises in the region of the uterine cornu and from there may migrate to the external os of the cervix being confined primarily to the endometrium with varying degrees of myometrial involvement. The growth may also advance rapidly through the wall of the uterus

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and by lymphatic dissemination soon infect the aortic group of glands by way of the ovary and infundibuliform lymphatics. The slowly growing tumor frequently reaches considerable size, with resulting enlargement of the uterus due to an intracavitary as well as myometrial invasion. It can be readily seen that an enlarged uterus not caused by an associated myoma denotes an advanced lesion with poor prognosis. The above statement is not always the rule; the young, active lesion, with a normal sized uterus, may have more extensive glandular invasion than that observed with the large uterus.

The advanced lesion may be associated with ascites due to generalized carcinomatosis resulting from transmigration of the growth through the myometrium with fragmentation of the papillary excrescences. The senior author has seen such late manifestations in two women who refused investigative curettage. When they were first seen the pelvic examinations were normal; however, on subsequent investigation months later, the developing abdominal distention proved to be due to ascites. At laparotomy, both patients showed extensive diffuse malignant implants originating from the growths on the surface of the uterus. Frequent paracentesis was necessary for comfort and cycles of deep roentgen therapy proved of no avail.

With the increasing number of women applying for investigation, the incidence of adenocarcinoma in relation to carcinoma of the cervix seems to be increasing. This increase has been particularly noted during the past few years and is the result, in a large measure, of increased educational programs developed under the aegis of the American Cancer Society and the Federal Government. With us the ratio is approximately 1 to 5.

It is usually stated that adenocarcinoma occurs more frequently in the nulliparous woman than in the multiparous. However, our studies show that 64.6 per cent of the patients had borne children, whereas 35.4 per cent were barren. This lesion also occurs as a rule in the more aged and it should be noted that 85 per cent were present during the menopause or thereafter and the remaining during the childbearing years. Our youngest patient was 23 years of age, the oldest 78.

The authors feel that emphasizing the occurrence of malignancy in specific age groups could be harmful for the physician may feel that the youth of the patient seeking aid for painless bleeding would preclude the possibility of corpus carcinoma and therefore not advise a diagnostic curettage.

In this study, 124 patients seen between 1932 and 1947 have been reviewed. The analysis according to age groups is as follows:

AGE	NUMBER	PER CENT
Under 35	5	4.0
35-45	10	8.1
46-60	62	50.0
61 or over	45	36.3
Age unknown	2	1.6
Total	124	100.0
The age of the youngest		23 years
The age of the oldest		78 years
The average age		55.9 years

It has been stated that the incidence of corporeal carcinoma is about equal in the white and Negro races. Our statistics show that this lesion occurred in 117 whites as compared to 6 in the Negro race. In one, the race was not mentioned. The only explanation we can offer for this wide variant is that the vast majority were private patients. This finding is of interest, however, for our

gynecologic clinic is predominantly of the colored race and if the incidence is equal there should be a greater number of blacks. Of the 124 patients studied, approximately 10, or 8 per cent, were of the Jewish race.

Differential Diagnosis

Curettage is the sine qua non in the diagnosis of corpus carcinoma. Conditions which produce painless bleeding with a normal pelvic examination are not too numerous; however, hyperplasia of the endometrium and other forms of dysfunctional bleeding are the most frequent lesions that have to be excluded. At times, atypical forms of endometrial hyperplasia are extremely difficult to differentiate from adenocarcinoma as brought out by Novak[1] in a recent publication. If doubt exists, the condition should be treated as malignant.

Other causes such as endometrial polyps and submucous myomas may be the source of painless bleeding. This latter condition can frequently be diagnosed with the curette. With distortion of the uterine cavity resulting from myomas a satisfactory curettage is difficult due to areas of inaccessibility. On removal and inspection of the uterus after the most careful curettage, one is often amazed at the amount of untouched endometrium remaining.

Perforation is one of the accidents that may occur, especially in the atrophic menopausal uterus. Of course, if intracavitary radiation had been planned and this mishap occurs, radium should not be inserted, as the capsule may even be lost in the abdominal cavity. Such a situation has been reported which necessitated laparotomy for its recovery. We have perforated the uterus on a number of occasions with no untoward results. On one occasion when perforation was done, the laparotomy, which had previously been planned, made possible the inspection of the puncture wound and we were amazed at the small amount of free blood present. Obviously, if this had occurred in a subinvoluted uterus, the amount of bleeding might have been excessive and thus have necessitated a laparotomy.

Prognosis is dependent in a large measure on the clinical extent of the disease and on individual biologic factors that are not clearly understood. The size of the uterus, as already noted, may be helpful in prognosis; here the lesion is often slow growing, invading the myometrium and developing a large intracavitary mass. The lesion may be well advanced prior to the onset of symptoms and in spite of its duration may still be in the realm of operability.

Treatment

With us the treatment of carcinoma of the fundus is divided into two categories dependent upon the condition of the patient, namely the good risk group and the poor risk group.

Treatment of the Good-Risk Patient.—Our routine is as follows: Careful and thorough curettage is carried out under Pentothal anesthesia. We have never been enthusiastic concerning suction curettage. Frozen sections are immediately examined. However, permanent ones are also made, for we have noted on very infrequent occasions that the frozen section may be negative while the permanent ones are positive. This situation makes for embarrassment if the patient has been informed that no malignancy exists. It is best to wait for the permanent section report before making a positive statement.

When a definite diagnosis of malignancy has been determined, multiple applicators containing 10 to 25 mg. of radium are inserted into the uterine cavity until it is quite full. Great care is taken not to perforate the diseased uterine wall. Varying number of capsules are used depending upon the size and con-

formation of the uterine cavity. A total of 4,000 to 4,500 mg. hr. of radium is the usual dosage. However, with a large uterus this may be increased. The filtration is of platinum and iridium and is equivalent to 2 mm. of lead. The several tubes are removed in reverse order so that a "log jam" does not develop. This complication occurred in one instance with breaking of the attached string, and the removal of the free tube was accomplished with great difficulty by probing the uterine cavity under anesthesia. In many cases the intracavitary radiation was accomplished by the use of 100 mg. of radium in a tandem. It is obvious that with this method the distant lesion, or inaccessible one, when associated with a myoma does not receive adequate radiation for we know the lethal ray of radium may extend only 2 to 2.5 cm. from the focal point. Thus, the distant cells may receive insufficient radiation, whereas the center of the lesion may be overradiated. In order to obtain adequate irradiation, multiple sources are preferable, as shown by the work of Heyman and Benner. Their method consists of introducing small amounts of radium into the uterus until the cavity is completely filled. The results with this method as compared with those obtained with the intrauterine tandem are striking and will be noted below.

From 1914 to 1933, a total of 354 patients were irradiated with radium in tandem using 35 to 45 mg. From this group the five-year survival rate was 45 per cent. Now compare these results with those obtained from the multiple source plan. From 1934 to 1939, a total of 316 patients was treated with a sufficient number of weaker tubes to fill the uterine cavity completely. By this multiple-source method, the five-year survival rate was 65 per cent. The above statistics are quoted from Arneson, et al.[2] During the period of intracavitary radiation, elevation of temperatures is carefully observed and if there is a sustained elevation to 102° F. radium is removed even before the completion of the application has been reached. Cellulitis and even peritonitis may result from intracavitary therapy. If the uterus is enlarged and there is an associated malodorous discharge, a preliminary cycle of deep roentgen therapy of 4,500 r. may be advantageous for the organ then regresses as does the intracavitary growth and the virulence of the infection tends to abate. This preliminary ray therapy is of especial value when dealing with a large submucous myoma which distorts the cavity and makes efficient radium application difficult or impossible.

Four to six weeks following radiation therapy, a panhysterectomy and bilateral salpingo-oophorectomy are performed. The most propitious time for this procedure is when the radiation effect is optimum. Obviously, this point is difficult to ascertain; one has to deal with many factors, such as cell sensitivity, biologic variation, the size of the lesion as well as of the uterus, etc. If the operative procedure is postponed many more weeks, increased fibrosis with loss of planes of cleavage comes about. Occasionally, rather dense adhesions are encountered binding down the pelvic organs. Some writers feel that radiation tends to increase the operative difficulty as a result of augmented bleeding. The individual variation is so marked that it is difficult to support such an opinion. Undoubtedly, the radiated, postmenopausal uterus undergoes increased obliterative endarteritis and there is a minimal amount of operative hemorrhage, whereas when dealing with a subinvoluted uterus prior to the menopause, bleeding may be far more profuse.

Approximately four to six weeks following the laparotomy, a cycle of deep ray therapy of 8,000 r. may be given. This procedure was carried out in 21, or 64.4 per cent of the cases studied. If definite metastasis outside the uterus is found, the subsequent cycle of ray therapy is of definite value, otherwise its efficacy is doubtful.

Treatment of the Poor-Risk Group.—The important conditions placing the individual in this category are as follows: advanced age with general debility, severe renal disease, hypertension with marked cardiac pathology, and obesity. With increasing experience the mechanical difficulty, occasioned by obesity, has become less of a problem. The main essential in the treatment of the very obese patient is a satisfactory ansthesia, preferably by the spinal route. However, if this is not feasible, cyclopropane with curare gives excellent relaxation. We have successfully operated on a number of patients over 250 pounds in weight with little difficulty. Once a positive diagnosis is made by curettage, intracavitary radiation is carried out as described above, the average dosage being between 4,000 and 4,500 mg. hr. using the multiple source technique. Following intracavitary radiation, a cycle of deep roentgen therapy is carried out until a dosage of 8,500 r. has been attained. As stated above, if the uterus is definitely enlarged with a protruding intracavitary growth, a cycle of roentgen therapy before the intracavitary radium is of value as the resulting regression makes for better radium application. We feel that the multiple-source technique is preferable to applying the radium in tandem as has been the custom. The advantages are obvious; for by this method better coaptation between radium and the growth is accomplished. As yet sufficient data have not been accumulated to present a comparative study of these two methods, but several reports, notably the one by Heyman, noted above, strikingly support this opinion.

The comparative results obtained between the good-risk and poor-risk groups over the period 1932 to 1942, were as follows: This study is based on 66 patients. Unfortunately 18 patients could not be included due to inadequate therapy and follow-up. Of this group of 66 patients, 32, or 48.5 per cent, were treated with intracavitary radiation followed by panhysterectomy and bilateral salpingo-oophorectomy. The five-year survival rate was 84.4 per cent with 27 patients living and well. There were five deaths during this period, or a rate of 15.6 per cent. The remaining number of patients, namely the 34 in the poor-risk group, were treated by radiation alone, i.e., intracavitary radiation followed by a cycle of deep roentgen therapy. Of the 34 patients treated, or 51.5 per cent of the total, there was a survival of only seven patients, a percentage rate of 20.6 per cent, twenty-seven, or 79.4 per cent dying from malignancy.

The survival rate of 20.6 per cent obtained by radiation is a poor showing when compared to the results of Heyman. He had a five-year survival rate of 45 per cent with the tandem method of therapy. With the multiple-source technique the survival rate for the same period was 65 per cent. It is fair to deduce, I believe, that if all the patients in the series, i.e., the good-risk and poor-risk, had been treated by intracavitary radiation, the survival rate would have been much higher. See Table I.

From a study of the figures in Table II, it is noted that the greater the maturity of the tumor, the greater the five-year survival rate. The highest rate of salvage was found in the differentiated grade I and II lesions.

TABLE I. FIVE-YEAR SURVIVAL RATE ACCORDING TO TYPE OF THERAPY

Total Number of Patients Treated 1932-1942	84
Number With Inadequate Follow-up and Treatment	18
Number of Patients in This Study	66

TREATMENT	TOTAL NO.	PER CENT	FIVE-YEAR SURVIVAL	PER CENT	DIED OF MALIGNANCY	PER CENT
Combined	32	48.5	27	84.4	5	15.6
Radiation alone	34	51.5	7	20.6	27	79.4
Operation alone	0		0		0	
Total	66	100.0	34	51.5	32	48.5

TABLE II. RELATIONSHIP BETWEEN MICROSCOPIC CLASSIFICATION AND FIVE-YEAR SURVIVAL RATE

Total Number of Patients Treated 1932-1942	84
Number With Inadequate Follow-up and Treatment	18
Number of Patients in This Study	66

GRADE	TOTAL NO.	PER CENT	FIVE-YEAR SURVIVAL	PER CENT	DIED OF MALIGNANCY	PER CENT
I	7	10.6	7	100.0	0	
II	27	40.9	16	59.3	11	40.7
III	13	19.7	4	30.8	9	69.2
IV	12	18.2	5	41.7	7	58.3
V (Adeno-acanthoma)	0		0		0	
Unknown	7	10.6*	2	28.6	5	71.4
Total	66	100.0	34	51.5	32	48.5

In order to determine the efficiency of the intracavitary radiation, a histologic study of the uterus, tubes, and ovaries was carried out. Multiple sections were obtained and suspicious areas in the uterine wall were even more thoroughly studied. In this group the uteri and adnexa of 67 patients were available for study, all of the patients having received a preoperative course of intracavitary radiation of 4,000 to 4,500 mg. hr. Of this total number, twenty-one, or 64.4 per cent, also received a cycle of deep roentgen therapy of 8,000 r. from four to six weeks following the panhysterectomy.

What are the histologic changes observed following this type of therapy? Nineteen, or 28.5 per cent, of the uteri and adnexa showed no residual malignancy. An analytic survey of the histologic gradings of this group is of interest and here the findings are as follows:

Grade I—occurring in 7 patients.
Grade II—occurring in 5 patients.
Grade III—occurring in 2 patients.
Grade IV—occurring in 1 patient.
Grade V—Adeno-acanthoma—occurring in 3 patients.
Unknown —occurring in 1 patient.

In this group there is the same postradiation reaction, namely complete destruction of the malignant growth. It would seem that the maturity or immaturity of the lesion is not of prime importance in the destructive reactions obtained. There are obviously other factors that must be considered, i.e., the size and age of the lesion, the size and conformation of the uterine cavity, the presence of infection, the proper coaptation of radium to the growth and, of the greatest importance, tissue sensitivity.

The histologic gradings of the 67 patients studied now follows:

Grade I—occurred in 15 patients.
Grade II—occurred in 25 patients.
Grade III—occurred in 13 patients.
Grade IV—occurred in 9 patients.
Grade V—Adeno-acanthoma,—occurred in 4 patients.
Unknown —one not recorded.

From this study it can be seen that in 59 per cent of the specimens investigated the histologic pattern was in the more differentiated grades.

The group in which residual carcinoma is found may be analyzed as follows: of the total number studied there is evidence of malignancy in 48, or 71.7 per cent. Extension into the myometrium is observed in 31, or 64.5 per cent. In 17, or 35.5 per cent, the growth is confined to the endometrium. Metastatic

invasion was found in the tube in four patients whereas the ovary was involved in three. An interesting observation frequently seen is the high incidence of uterine myomas associated with carcinoma of the corpus. In this series 27, or 40.3 per cent, of the uteri contained these benign lesions. Some are of the opinion that the projecting submucosal growth may be an irritant to the endometrium with resulting malignant changes. As is commonly known, there is a high association of hyperplasia of the endometrium concomitant with uterine malignancy. Hyperplasia results from hyperestrinism and some writers have attempted to prove rather unsuccessfully that uterine myomas are produced by the same hormonal stimulus. When one sees atypical borderline areas of hyperplasia where the malignant status is uncertain, one cannot help but be impressed by the possible carcinogenic effect of the overabundant estrogenic factor.

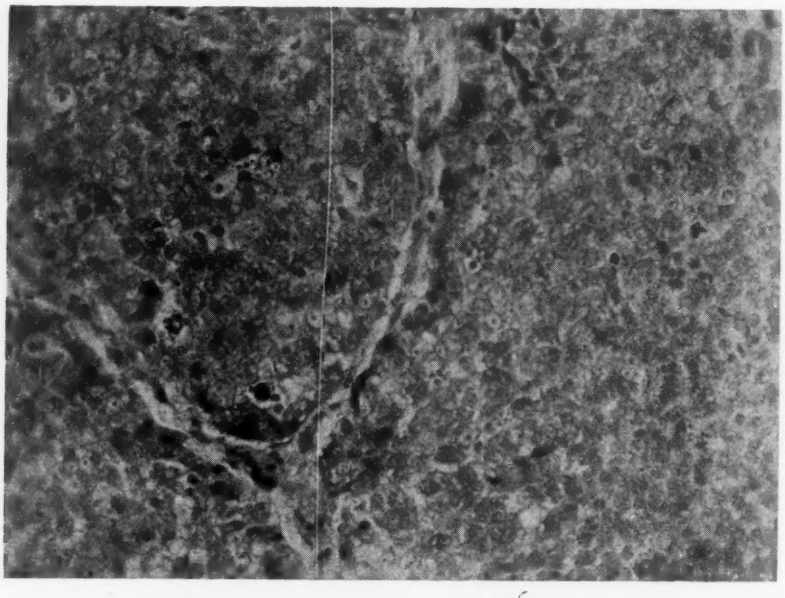

Fig. 1.—Marked anaplasia, Grade IV. Adenocarcinoma curettage.

Variation in Tissue Reaction

On completing a study of the various reactions and results observed in the radiated uteri, one is struck by the marked variation in tissue response. If the growth is confined to the endometrium and there is satisfactory radium application and sensitivity, one can expect a good reaction, as evidenced by absence of viable cells.

This is so well depicted in the case of Mrs. R., aged 43 years, who was observed thirteen years ago for painless vaginal bleeding of about three months' duration. The pelvic examination was normal and a diagnostic curettage was done with the tentative diagnosis of hyperplasia having been made. The tissue obtained was not the amorphous jelly-like material such as that seen with hyperplasia but was of definite form and solid in consistency (Fig. 1). A clinical diagnosis of adenocarcinoma was made and confirmed by histologic study. A markedly anaplastic growth with no cell pattern was seen. Intracavitary radiation was then carried out, the radium being inserted in tandem, and a total dosage of 4,500 mg. hr. was given. Six weeks later a bilateral salpingo-oophorectomy and panhysterectomy were performed. A practical point of value is the clamping of the isthmic portion of the tubes. This precludes the

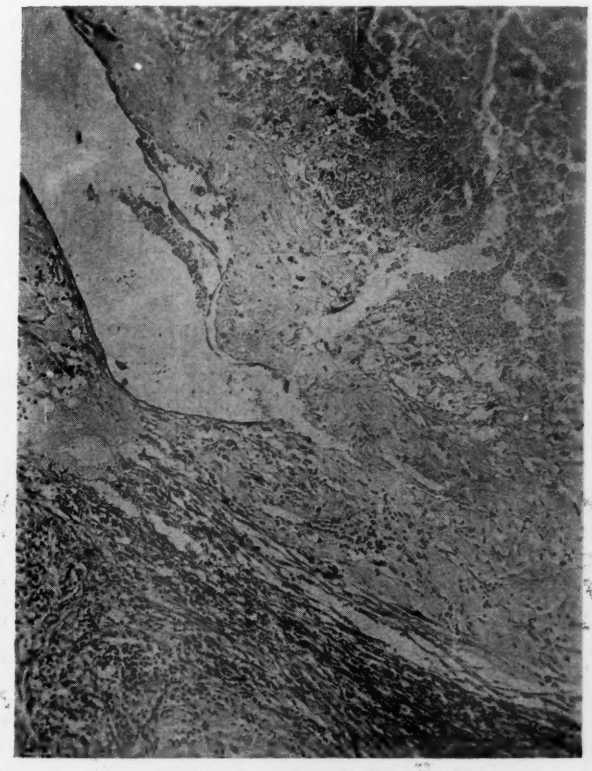

Fig. 2.—The same tumor as seen in Fig. 1, post radiation, 4,500 mg. hr. Coagulum with complete destruction of the malignant cells.

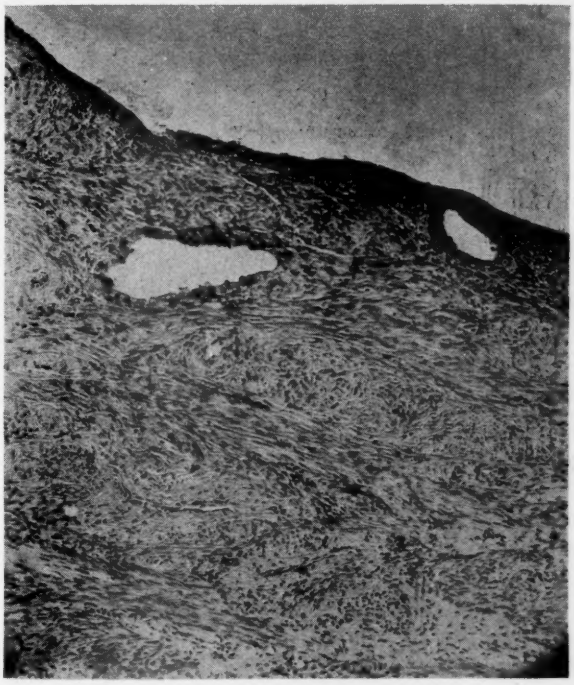

Fig. 3.—A photomicrograph of the myometrium in the same tumors as seen in Figs. 1 and 2. The endometrium is absent and two normal glands may be seen.

possibility of cells being expelled into the peritoneal cavity during manipulation of the uterus. When the uterus was opened, a circumscribed lesion about 1.5 to 2.0 cm. was found in the region of the right cornu. The tissues were quite pale and the myometrium appeared normal. Microscopic sections showed complete regression of the growth, no viable cells were seen (Fig. 2). The endometrium was absent and in the myometrium two glands were found which showed no evidence of malignancy (Fig. 3). The postoperative convalescence was normal and frequent examinations since then have shown no evidence of disease. If metastasis had occurred, it would most likely have been seen in the vault of the vagina giving the appearance of granulation tissue.

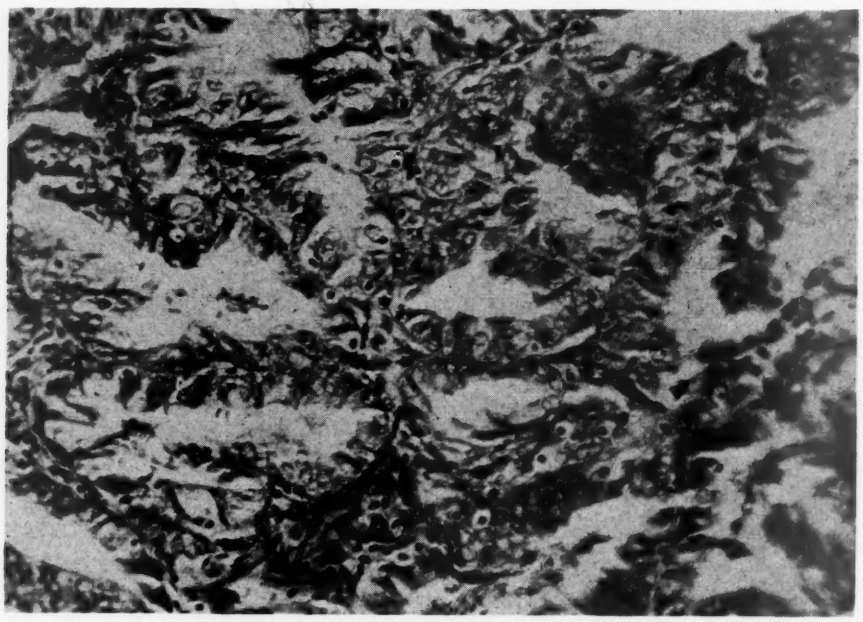

Fig. 4.—Adenocarcinoma, Grade II. Curettage.

Biopsy of any suspicious lesion in the vault is most essential. If radiation is indicated, great care must be exercised to preclude the possibility of fistula formation. In one patient, granulation-like tissue was seen in the vault. This was treated by radiation with a resulting rectovaginal fistula. Unfortunately the surgeon failed to obtain a biopsy prior to the treatment. When one was taken subsequently, no malignancy was found. If it had been known that no malignancy existed, a simple cauterization of the granulation tissue would have sufficed.

In other uteri studied with similar endometrial involvement, varying degrees of cellular devitalization may be seen. These changes range from complete necrosis to cells that show comparatively few changes. These latter, as a rule, are more distant from the focal point of radiation. The common findings, when the growth is in the endometrium, are necrosis, coagulum formation, cellular enlargement with nuclear destruction, fragmentation, and giant-cell formation. Phantom cells also may be seen (Figs. 4 and 5).

The above description is in contrast to that observed when the growth involves the myometrium; here it would seem the cells are somewhat protected by the filtration engendered by the overlying fibromuscular tissue of the uterine wall. These cellular changes are well depicted in Figs. 6 and 7.

A well-known example of tissue selectivity is evidenced in the successful treatment of benign uterine bleeding, which is accomplished by cessation of ovarian activity produced by intracavitary radiation. With us the spaying dosage is 2,000 mg. hr., less than half that used in treating intracavitary carcinoma. The follicular system of the ovary must be extremely sensitive to radiation when one observes its complete dissolution under comparatively small radium exposure at a distance of 4 to 6 cm., always provided the ovary is sufficiently dependent and near the uterine wall. Colwell and Russ[3] in their work on *Radium, X-ray and the Living Cell* report an excellent example of selective behavior, i.e., the action of heavy gamma-ray doses of radium upon the kidney.

Fig. 5.—The same growth as seen in Fig. 4, post radiation, 4,500 mg. hr. Coagulum with complete destruction of the malignant cells may be seen.

"Here it was possible to observe in one and the same microscopic field that the cells of the convoluted tubules had undergone vacuolation and degeneration while the conducting tubules were apparently but little affected. It is obvious that the amount of radiation to which both types of cells were exposed must have been practically the same." The explanation of this varying reaction may be dependent on the difference in the embryologic origin of these cells. The

conducting, or collecting, tubules are derived from outbuddings of the ureter which arises from the primary excretory duct, whereas the convoluted tubules are mesenchymal in origin and are of a more specialized nature.[4]

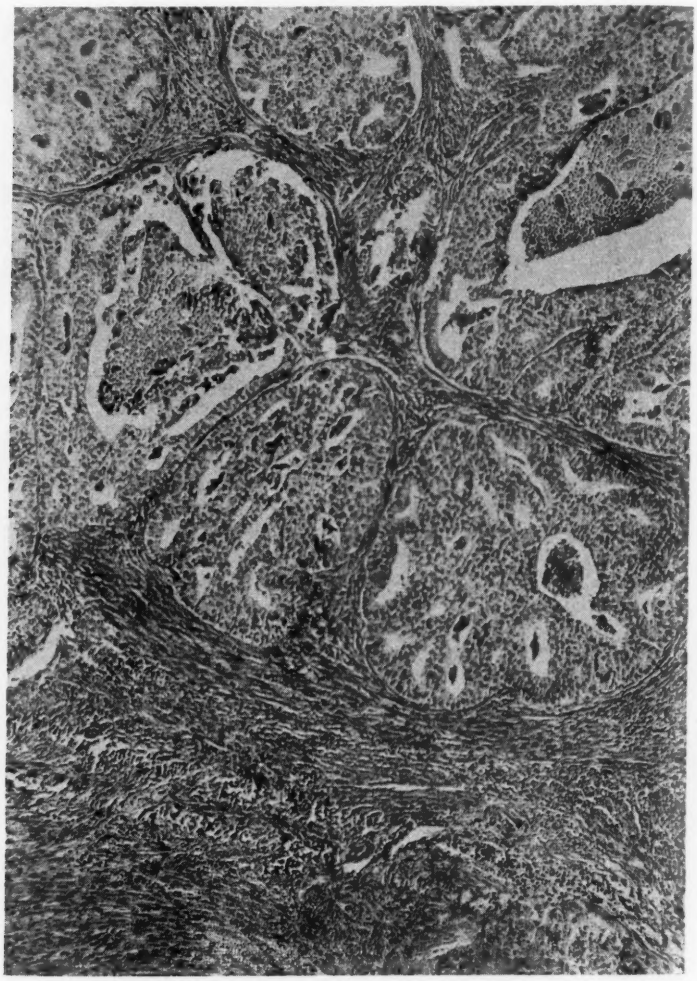

Fig. 6.—Malignant cells seen in the myometrium, post radiation.

Summary and Conclusions

1. The five-year survival rate of 32 patients treated with intracavitary radium and panhysterectomy is 84.4 per cent.

2. The five-year survival rate of 34 patients treated with intracavitary radiation and a cycle of deep roentgen therapy, 8,500 r., is 20.6 per cent.

3. Twenty-one, or 64.0 per cent, of the patients, received an additional postoperative cycle of deep roentgen therapy. The complete therapy in this group consisted of intracavitary radiation, 4,500 mg. hr., panhysterectomy, and a postoperative cycle of deep roentgen therapy, 8,500 r. This added postoperative ray therapy is definitely indicated when extrauterine metastasis is observed. Otherwise it is not obligatory.

4. There was no operative mortality and no untoward sequelae were noted during convalescence.

5. No planned treatment by surgery alone was performed.

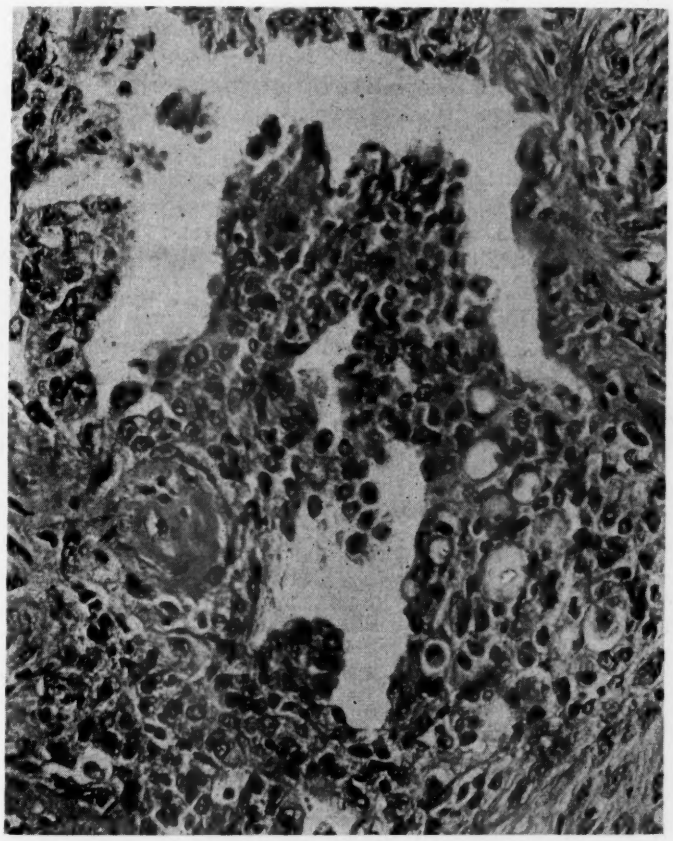

Fig. 7.—Polyp, post radiation, showing obliterative endarteritis, malignant cells, and vacuolization.

A Summarized Histologic Study of Radiated Uteri as to Residual Malignancy

1. The uteri and adnexa of 67 patients were available for study.

2. Nineteen, or 28.5 per cent, of the uteri and adnexa showed no residual malignancy.

3. Residual carcinoma was found in 48, or 71.7 per cent.

4. Extension of the growth into the myometrium was noted in 31, or 64.5 per cent, whereas the process was confined to the endometrium in 17, or 35.5 per cent.

5. Tubal involvement was found in four patients and the ovary was affected in three.

6. Uterine myomas were associated with corpus carcinoma in 27 patients, or 40.3 per cent.

From this study the authors are of the opinion that intracavitary radiation by multiple sources, followed by panhysterectomy and bilateral salpingo-oophorectomy is the procedure of choice in the treatment of corpus carcinoma. From the histologic study of the material and from the high observed incidence of residual malignancy the authors feel that panhysterectomy is of the greatest importance. Although residual carcinoma was found in 48, or 71.7 per cent, of the specimens studied, the vast majority of the residual cells shows evidence of radiation reaction even though some of them appeared quite normal.

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622 MEDICAL ARTS BUILDING

Discussion

DR. JOHN L. McKELVEY, Minneapolis, Minn.—There is evidence that the time is ripe for a critical evaluation of some of the conclusions which are presently being drawn in regard to the treatment of adenocarcinoma of the endometrium. Dr. Hundley's study brings some of these problems into focus.

The essayist has raised these problems of the value of x-ray, of intrauterine radium irradiation, and of surgical attack. It is astonishing that students of the subject have come to such diverse conclusions.

One gathers that the author is somewhat skeptical of the effectiveness of x-ray as a method of applying irradiation energy, although he uses it. A considerable part of the American literature would urge preliminary x-ray irradiation as the method of choice. This should be critically examined. It is impossible to tell from the skin dosages which are so often used for reporting just what dosage was obtained at depth. However, a tumor dose at depth of 3,000 to 4,000 tissue roentgens is the maximum that can be given over the usual four-week period. This represents about 1,500 to 2,000 roentgens in terms of biologic effect after recovery rate for comparison with the radium irradiation which is given over only a few days. With combinations of x-ray and radium or with radium alone which supplies about six times this dosage to the uterine cavity, a large proportion of the adenocarcinomas escape destructive effects. Stowe reported on the University of Minnesota material and showed 50 per cent residual tumor after x-ray and radium irradiation. Hundley has shown 71 per cent residual tumor. McLennan reported on a series which was purposefully treated and studied to evaluate the effect of x-ray and concluded that it added nothing to end results. An expensive procedure is added and from four to eight weeks of the duration of life of the tumor is added.

Very large doses of irradiation energy can be given by intrauterine radium in adequate distribution. In contradistinction to x-ray, where only homeopathic doses can be given to what must be considered a relatively radioresistant tumor, the use of the inverse square law to advantage by the use of intrauterine radium will, at least for the surface of the cavity, satisfy the theoretical requirement of 7 to 10 E.S.D. or 7,000 to 10,000 gamma roentgens. But studies as that of Stowe have shown that a maximum of 50 per cent of these irradiated uteri are histologically free of tumor. As such it is useful for those patients in whom surgery cannot be carried out. It is not too clear as to just what we are trying to accomplish by irradiation in those patients who can be treated surgically and we are now collecting a series without preliminary irradiation for comparison.

It is difficult from the reported studies to get any clear idea as to what has really been accomplished. The series are small so that statistical significance is most often lacking. The results of irradiation or of surgery or of both are too often modified by the type of material which is exposed to the specific form of treatment. The further one extends the indications for surgical attack, the smaller the proportion of surgical cures will be produced and vice versa. The question arises as to whether or not an increase in the proportion of patients treated surgically will increase the total recovery rate of the whole group. There is reason to hope that it will, as evidenced by the fairly continuous reporting of 20 per cent recovery rate with irradiation alone and 75 to 80 per cent recovery rate when the surgical attack is used with the customary indications. We have satisfied ourselves that the surgical rate can be increased with reasonable safety. Prior to 1939, 33 per cent were surgically treated. From 1939 to 1942, this rate was doubled. From 1942 to the present, the surgical rate is 75 per cent. The effectiveness of this is still to be proved by a large enough series but it is promising enough to appear to justify agreement with the essayist's statement that "panhysterectomy is of the greatest importance."

DR. CONRAD COLLINS, New Orleans, La.—We would like to comment on the results obtained in Charity Hospital from 1938 to 1943. The reason we surveyed these years is because the new hospital was opened in 1938 and the supply of radium was increased. During this five-year period there were 41 cases treated either by irradiation or irradiation and surgery combined. Counting two untraced patients as dead, in a total of 30 cases treated by irradiation and surgery, there was a five-year survival of 70 per cent. The majority received radium applied in tandem, using three 15 mg. tubes, two applications five to seven days apart, followed by total abdominal hysterectomy and bilateral salpingo-oophorectomy. Of the cases treated by irradiation alone, the same dosage of radium was used as well as x-ray, usually 10,000 r. in air; a five-year survival of 29 per cent was obtained. We do not believe that radium and surgery are competitive in treatment of carcinoma of the cervix but that they are complementary and supplementary.

Of the cases shown here, we would like to report a group of 25 cases in which surgery alone was used, in the years 1942 to the present. Surgery did not consist of any extensive operation. Bilateral salpingo-oophorectomy was performed and a generous amount of cuff removed. We do not subscribe to surgery alone. Following surgery in from three months to three years, seven showed recurrence or implantation. Of these, three implantations were in the vaginal cuff, one in the abdominal wound, and three were definite recurrences in the vaginal cuff.

We agree with Dr. Hundley that curettage will not show carcinoma in some cases. However, we believe, in our area at any rate and particularly in our service, that curettage was not used often enough. Occasionally, during postmenopausal bleeding, the patients were operated on without a curettage and I am certain that if they had had a curettage before laparotomy some of these results would have been improved.

DR. FRANKLIN L. PAYNE, Philadelphia, Pa.—Among the many interesting points in this presentation is the statement that over 70 per cent of the uteri that were removed following intracavitary irradiation showed residual cancer. Therefore, much remains to be done in the field of radiation therapy for corpus carcinoma, whether it is to be used as a

preliminary to surgery or as the only therapeutic measure. Paterson states that successful treatment of malignancy depends upon the administration of a tumor lethal dose within the tolerance limits of normal tissues. The problem is one of distributing the sources in such a way as to produce homogeneous radiation throughout a certain volume and then of measuring the dose produced thereby.

In attacking this problem at the Hospital of the University of Pennsylvania, we are experimenting with a slight modification of the Crossen wire technique of intracavitary distribution, which is checked by x-ray examination following each application. The x-ray plates serve three purposes: first, that of detecting possible perforation of the uterus. The accompanying slides shows the only instance of this accident that we have experienced. This perforation was detected within three hours of the radium application and the applicators were removed with no untoward results. Second, the need to see the distribution of the radium sources. In the presence of advanced corpus cancer we believe it is unwise to attempt to administer the desired dose of radiation at one sitting because of the dangers of massive local necrosis and of injury to the contiguous structures. Repeated applications tend to diffuse the ultimate dosage and to avoid what the radiation therapists speak of as "hot spots."

In the case to which I referred the radium was placed fairly evenly throughout the uterine cavity and the attempt to place one or two of the applicators across the top of the fundus was reasonably successful.

Now we reach the most important question: How much irradiation did this uterus receive in terms of tissue dosage? This introduces the third purpose of the x-ray plates: from the two preceding exposures a composite diagram was made to depict the distribution that was obtained in both applications. The measurement and expression of tissue dose in terms of gamma roentgens is an involved problem that is laden with much mathematics and many variables. Our radiation therapeutists believe, however, that an approximate estimate is feasible and we are indebted to Drs. Eugene Pendergrass and John Freed of the Department of Radiology for their invaluable help and guidance in this work. While we do not know the exact tumor lethal dose of radiation for adenocarcinoma of the uterine corpus, work upon other types of malignancy in other locations suggests that it ranges from six to ten thousand gamma roentgens. The tissue dose approaches that which we believe to be cancerocidal throughout the greater part of the uterine wall. The undertreated areas lie in the external cornual regions and in the cervix—a defect that has been corrected in subsequent applications.

This work is laborious and time consuming but we believe that it has sufficient clinical possibilities to justify its continuation. If it proves to be practical it may lead to the following general procedure: multiple small source intracavitary application by the gynecologist, then transfer to the radiologist for x-ray plates and determination of the length of time that the radium is to remain in place to produce the desired tissue dose throughout the uterus. While this may be a fantastic dream, we cannot escape the thought and the hope that the full usefulness of intracavitary irradiation has not been explored completely. By thinking, not in terms of milligram hours but in terms of tissue dosage to be administered by the even distribution of multiple small sources, it is likely that we can do much to increase the effectiveness of intracavitary irradiation in the treatment of cancer of the uterine corpus.

DR. THOMAS C. PEIGHTAL, New York City.—Dr. Hundley has maintained a splendid record of five-year cures, that is, of the cases that he was able to follow, which surpasses all but one or two of the records in the literature.

Dr. Hundley has noted that an ever-increasing number of women are applying for examination following menstrual irregularity at or near the menopause so that the proportional incidence of adenocarcinoma as compared with cervix carcinoma in his clinic has risen to a ratio of 1 to 5. A majority of his cases occurred in multiparas (64.6 per cent); 85 per cent were at or after the menopause, and the average age was 55.9 years, only 36.3 per cent being over 60 years. The low incidence of corpus cancer in the Negro race is

interesting (117 whites to 6 Negro women). Dr. Hundley notes that favorable prognosis varies according to the size of the cancer-bearing uterus, to which all must agree.

For his ideal treatment of the good-risk patient, Dr. Hundley irradiates the fundal cavity with multiple source applicators and his dosage of 4,000 to 4,500 mg. hr. of irradiation seems adequate. This is followed by panhysterectomy with bilateral salpingo-oophorectomy six weeks later and in the majority of cases (21 out of 32) a pelvic cycle of roentgen therapy for a total of 8,000 r. was given four to six weeks after laparotomy. In this group he has obtained the excellent result of 84.4 per cent five-year cures. This is a determinate percentage based on just the total cases followed (32 in number).

For the poor-risk group (34 in number), Dr. Hundley uses 4,000 to 4,500 mg. hr. of intracavitary irradiation followed, or in some instances preceded, by roentgen therapy of 8,500 r. and in this group he has obtained only 20.6 per cent five-year survivals, but it must be emphasized that these were all poor-risk patients.

Dr. Hundley has shown us the percentage of five-year survivals according to the various pathologic gradings. Among these, 52 per cent of his cases were in Grades I and II and in these he obtained 68 per cent five-year survivals by all methods of treatment. One wishes that he had noted his end results on the basis of pathologic grading for each of his two types of treatment, i.e., irradiation alone and irradiation plus surgery.

In the histologic study of uteri removed, it is to be noted that in 19 (28.5 per cent) there was no residual malignancy after the preliminary irradiation. Since these favorable results were found in all pathologic grades, he feels that other factors such as clinical stage of disease may be the more important factor in growth eradication by intra-cavitary irradiation. In the 71.1 per cent showing residual cancer after irradiation, inability to obtain accurate application of the multiple source capsules, because of the presence of myomas or extensive myometrial involvement, seems to have been the chief cause of failure. A splendid histologic study of tissue response for growth, both in the endometrium and myometrium, has been undertaken and is carefully evaluated.

We have ready for publication a report of 157 cases of carcinoma of the endometrium from the Roosevelt Hospital. The average age incidence has been 56 years, only 18 per cent have occurred in the Negro race, and 58 per cent in multiparas. The average age at menopause has been 49 years and 36 per cent had myomas.

It is obvious from our own experience, when analyzed from the standpoint of stage of lesion and grade of malignancy, that preoperative irradiation plus hysterectomy offers no advantage over hysterectomy alone in *early* lesions or in *low* histologic grade; and very little advantage in *advanced* lesions or *high* histologic grades. In support of this it is interesting to show a few slides of composite results from various clinics.

As the risk of being declared a radical we submit the question, "Can we go above 80 per cent five-year survivals by present methods of treatment?" Probably not because of nodal involvement and distant metastases.

We submit therefore that in good-risk patients it is likely that our best results in the future will be obtained from a more extensive hysterectomy, i.e., a wider excision of parametria with, where possible without undue risk, a lymphatic node dissection, particularly where nodes are obviously involved. Since the average age incidence of these patients is 56 years, more than is usually supposed of them are good-risk patients. True, many are obese, but for them we can envisage among the proponents of more radical surgery in corpus carcinoma even a three-stage operation of 1. wide hysterectomy; 2. several weeks later, an extraperitoneal lymph-node dissection by the inguinal approach on one side as described by Nathanson, Parrous, and Meigs; and 3. still later, a similar node dissection of the other side. Is it not possible that our best results may eventually come by such a procedure?

However, Dr. Hundley has obtained a very high percentage of 5-year survivals (84.4 per cent) by his method of treatment—radium plus hysterectomy in good-risk patients. This compares favorably with Dr. Norman Miller's series of 96 cases treated by preoperative roentgen therapy plus hysterectomy with a 77 per cent five-year survival, and more than

favorably with five-year results either from surgery alone, or from radium, x-ray, and surgery combined in all other clinics. Therefore, Dr. Hundley is to be congratulated for a most excellent paper and for his splendid results.

DR. LEWIS C. SCHEFFEY, Philadelphia, Pa.—I am still able to report a 100 per cent follow-up of all of the patients with fundal carcinoma seen in the Division of Gynecology, Department of Obstetrics and Gynecology, at Jefferson Medical College and Hospital since 1921, 207 in number.

In the case of the group of patients in whom radium, and radium alone, was used prior to surgery, our five-year and longer surgival figure is 85.2 per cent. This applies to 27 patients eligible for five-year statistics. In addition are 29 more patients, of whom 28 have survived from one to four years or a bit longer. Neither has there been a surgical mortality among these 56 patients. Thus, we have found from our experience that preoperative radium has added a great deal to our immediate and long-term survival record.

I will not go into details about this "planned technique" and its application, for our procedure has been published repeatedly in the past. I have never believed that the preliminary application of radium destroys all of the cancer, but it certainly attenuates its vigor and renders subsequent surgery safer and more effective, especially with respect to recurrence in the vaginal vault scar. This was not true of the methods used in the earlier days. I can subscribe substantially to many of the points that Dr. Hundley has brought out.

DR. GEORGE W. KOSMAK, New York City.—I desire to refer to a matter that may not bear directly on this discussion but which seems to me of considerable importance. As a result of the nation-wide propaganda for the early detection of cancer, there have been opened in many places in this country so-called "cancer detection centers." It must be acknowledged that the early diagnosis is one of the most important topics that should be considered in the attempt to eradicate this disease. It seems to me, however, that it would be desirable if organizations with authority, such as the American Gynecological Society, would develop certain standards of practice for the so-called "detection centers." It has become a very popular movement in many counties over the country to open these centers. Now my hesitancy about the value of some of these centers is based on a report that I received for publication a year ago in the JOURNAL, emanating from a contraceptive clinic in the neighborhood of New York City. As you know, this organization has been very desirous of exploiting the fact that they are able to detect a great many gynecologic conditions in giving contraceptive advice. To quote one result from this clinic: the author of the paper claimed that, within a certain period 3,000 patients had been examined and in only four cases were any lesions of the cervix detected that merited reference to a physician. There is something at fault there when we have such results from what might be expected from reliable observations. I am sure that every one who has practiced gynecology will subscribe to the fact that in 3000 cases examined there would be more than four with lesions that needed further investigation. I hope as a result of the papers and discussions presented some action will be taken through this organization or through the American Cancer Society to establish certain standards of examination for these various cancer detection centers.

DR. HUNDLEY (Closing).—I have nothing further of significance to offer. There are many pros and cons concerning this problem which we could debate ad infinitum. However, as the hour grows late and there are still several papers to be presented I will not detain you with irrelevant remarks.

Dr. McKelvey is to be congratulated on his splendid results with surgery alone. We feel that panhysterectomy can be performed with a high five-year survival rate provided that the microscopic pattern of the growth is of the mature type; we also feel that the operative results obtained are poor when the growth is of the anaplastic group.

In closing, I wish to state that I still feel that the combination treatment, i.e., intracavitary radiation followed by panhysterectomy, is the method of choice in the treatment of adenocarcinoma of the body of the uterus for by this method we have obtained an 84.4 per cent five-year survival rate.

FACTS PERTINENT TO A RATIONAL CONCEPT OF ABRUPTIO PLACENTAE*

R. A. Bartholomew, M.D., E. D. Colvin, M.D., W. H. Grimes, Jr., M.D., and John S. Fish, M.D., Atlanta, Ga.

(From the Department of Obstetrics of Emory University School of Medicine)

IT IS the purpose of this paper to restate facts which have heretofore admittedly supported a toxemic origin of abruptio placentae and to present additional facts strengthening this viewpoint.

The following clinical and pathologic evidences indicate that abruptio placentae is a manifestation of toxemia of pregnancy and is a phenomenon which may occur in any case of severe toxemia and interrupt the pregnancy before the convulsive stage is reached:

1. *The Frequent Occurrence of Symptoms and Findings of Toxemia Preceding Abruptio Placentae.*—

A majority of the cases of abruptio placentae shows typical clinical evidences of toxemia some days or weeks before hemorrhage and separation of the placenta terminate the pregnancy, i.e., increasing edema, headache, rising blood pressure, increasing albuminuria, arteriolar spasms in the retinas and increasing blood uric acid. The severity of the abruptio parallels not only the coexistence but particularly the severity of the toxemia.

Portes found an associated toxemia in 91.3 per cent of the cases of abruptio placentae in Couvelaire's Clinic.[1] Dieckmann[1] found that 69 per cent of cases of abruptio placentae at the Chicago Lying-in Hospital had associated toxemia. In a former study[2] evidence of toxemia of pregnancy was found in 33 of 61 cases analyzed. A study of the literature reveals many analyses emphasizing this association.[13, 14]

Due to the fact, however, that a variable percentage of cases, particularly of the fulminating type, fails to show clinical evidences of toxemia, there has been no unqualified acceptance of a toxemic origin of abruptio placentae. Evidence which establishes a toxemic basis in this group of apparent exceptions will be presented later in discussing the pathology of the condition.

2. *Simultaneous Occurrence of Eclampsia and Abruptio Placentae.*—

Occasionally, toxemic patients are affected by abruptio placentae and eclampsia simultaneously, as in Cases 28 and 42, in the present series. This indicates that toxemia is probably the common etiological factor. Pathologic evidence leads further support to this view.

Furthermore, it is not uncommon to find a subclinical mild degree of abruptio placentae in the placentas of patients who have eclampsia.

3. *Similarity of Necropsy Findings in Eclampsia and Abruptio Placentae.*—

The similarity of the pathologic findings in the liver, kidneys, brain, and other vital organs indicates an etiological agent common to both conditions, but with a greater predilection to damaging effects on the mechanism of blood coagulation, hemorrhagic manifestations, and vascular damage, in abruptio placentae.

*Read at the seventy-first annual meeting of the American Gynecological Society, Williamsburg, Virginia, May 24 to 26, 1948.

Necropsy: C. R., Hospital No. 304650, aged 32 years, gravida ii, para i; history of orthopnea and nocturnal dyspnea past several years; at seventh month of present pregnancy had sudden hemorrhage, estimated one pint; had developed edema and headache two days preceding; blood pressure 200/160, heart enlarged, moderately severe vascular disease, no spasms, numerous flameshaped hemorrhages in retina; albumin 2 plus; uterus tense, fetal heart not heard; diagnosis, abruptio placentae. Sedation and supportive treatment; spontaneous onset of labor and delivery, 1,640 Gm. slightly macerated fetus; 500 c.c. blood and old clots followed placenta, which showed indented area of premature separation but unfortunately not examined for infarction. Delivery followed by increasing orthopnea and dyspnea; one transfusion, continuous oxygen, rapid digitalization; blood pressure 220/160, pulse 128, development of pulmonary edema; sudden death in cardiac failure several hours later. Necropsy performed. Summary of findings: "Histologically, this patient showed the lesions diagnostic of toxemia of pregnancy"; arteriolitis with formation of fibrin thrombi in damaged arterioles, seen in kidney (thrombosis of afferent arterioles and infarction of glomeruli), also in terminal branches of hepatic artery and sinusoids of liver, and in pulmonary arterioles.

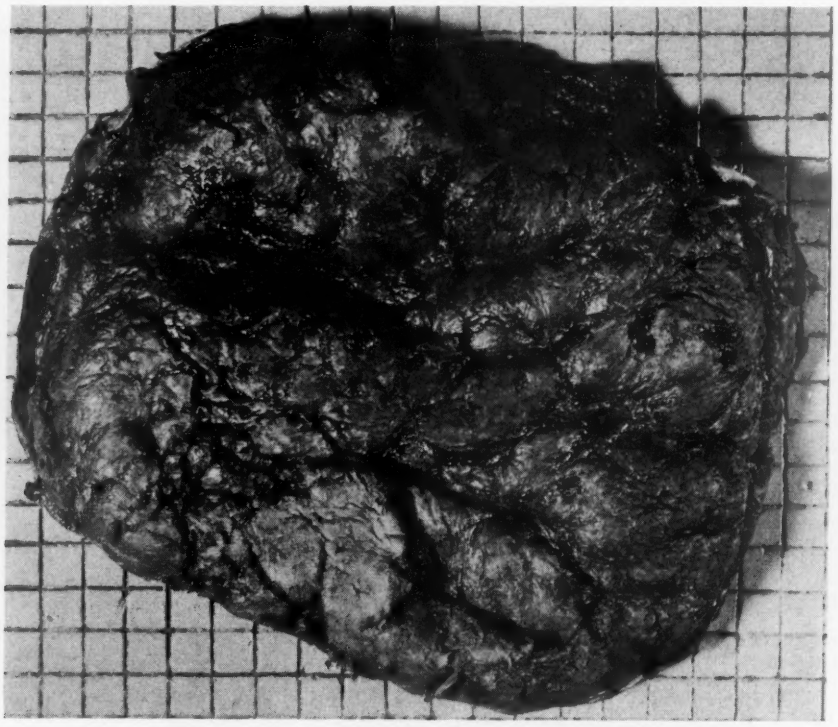

Fig. 1.—Abruptio placentae, Case 43; upper two-thirds dark due to acute hemorrhagic infarction; lower third normal.

The above facts constitute strong circumstantial evidence but have apparently not been regarded as sufficient to indict toxemia as the cause of abruptio placentae.

The following additional evidence establishing a specific pathology in the placentas, common to both eclampsia and abruptio placentae, should justify acceptance of toxemia of pregnancy as the etiological factor common to both.

4. *The Consistent Occurrence of Acute or Subacute Hemorrhagic Placental Infarcts in All Cases of Abruptio Placentae and Eclampsia, Identical in Both Gross and Microscopic Appearance.*—

Placentas from consecutive cases of abruptio and eclampsia from several of the local hospitals were saved over a period of a year. The following is a summary of the clinical and placental findings in a series of fifty placentas examined:*

20 cases of abruptio placentae
6 cases of eclampsia
2 cases of abruptio and eclampsia
4 cases of severe or pre-eclamptic toxemia
18 cases of normal pregnancy, included for comparative placental diagnosis.

50 total number of cases. No maternal mortality.

20 Cases of Abruptio Placentae:
15 or 75 per cent showed vascular disease (retinal examination).
12 showed shock, mild to severe.
9 had severe hemorrhage (estimated 800 to 1,200 c.c.).
11 had moderate hemorrhage (estimated 500 to 800 c.c.).
12 had tense uterus (eight not mentioned).
7 had unfavorable cervix (1 to 3 cm. in length) but were successfully induced by artificial rupture of membranes.
19 were fulminating.
9 babies stillborn; 3 neonatal deaths; one fetus aborted at 4½ months with associated abruptio; 7 babies survived. Fetal mortality 60 per cent.
14 had one to six transfusions. Average of 3.6 transfusions each.
6 did not require transfusion.
20 (100 per cent) showed well-defined early "E" infarction, which agreed with clinical diagnosis of toxemia.
20 (100 per cent) delivered spontaneously, following either spontaneous labor or successful induction.

6 Cases of Eclampsia:
1 showed vascular disease.
2 were fulminating.
6 (100 per cent) showed well-defined early "E" or "D" infarction which agreed with the clinical diagnosis.
1 stillbirth; 4 babies survived (1 baby chart missing). Fetal mortality 20 per cent.
6 (100 per cent) had spontaneous delivery after induction of normal labor.

2 Cases of Abruptio Placentae and Eclampsia Combined:
2 cases showed vascular disease.
1 case showed shock.
2 cases had moderate degree of hemorrhage.
1 case had tense uterus.
1 case had unfavorable cervix.
1 neonatal death; 1 baby survived.
2 cases showed well-defined early "E" infarction which agreed with clinical diagnosis.
2 cases delivered spontaneously.

4 Cases of Severe or Pre-eclamptic Toxemia:
4 showed well-defined "E" infarction (2 early "E," 2 late "E").
4 had spontaneous delivery.

18 Cases of Normal Pregnancy (Included for Comparison of Placental Findings):
No cases of vascular disease, shock, hemorrhage or fetal mortality.
6 cases showed no recognizable area of infarction.
8 cases showed questionable "E" infarction, in gross examination.
4 cases showed well-defined early "E" infarction, although clinically normal.

Summarizing these results, it was found that if the patient had eclampsia, abruptio, severe or pre-eclamptic toxemia, well-defined early or late "E" infarction of the placenta was always present (32 cases—100 per cent).

*The details of the clinical and placental findings in each case are omitted here for the sake of brevity, but are included in the reprints.

Nineteen of the abruptio cases and two of the eclamptic cases in this series, were so fulminating, that preceding clinical symptoms and findings were absent or mild, yet unmistakable infarction was present in the placentas in all cases and indicated an associated severe toxemia.

If the patient was clinically normal throughout pregnancy, or at the last prenatal visit, within two weeks of the onset of labor, six of the eighteen cases (33 per cent) showed no recognizable infarction.

The total number of toxic and normal cases in agreement with the placental findings was 76 per cent.

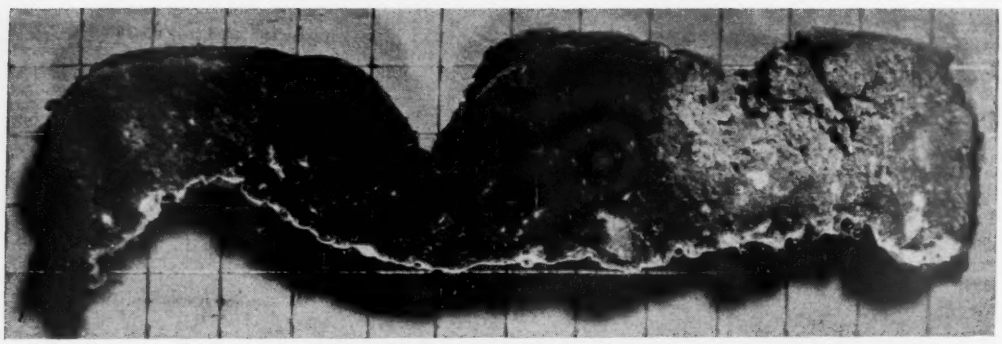

Fig. 2.—Strip from placenta of Fig. 1; sharp line of demarcation between confluent dark early "E" hemorrhagic infarction involving two-thirds of the placenta (to left), and the lighter normal placenta (to right).

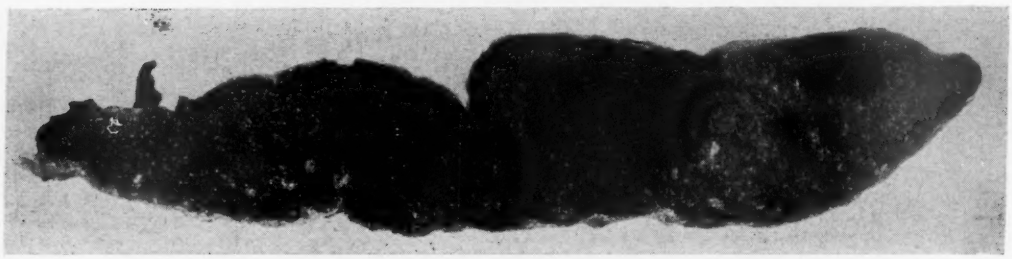

Fig. 3.—Abruptio placentae, Case 7; placental strip showing both confluent and isolated early "E" hemorrhagic infarction.

The four well-defined early "E" infarctions in clinically normal cases, may have been early infarctions, too early for recognizable clinical effect.

The eight questionable "E" infarctions in clinically normal cases may have been due to temporary partial obstruction by sphincters of the placental veins, just before or early in labor. Comment on these will be found in the discussion.

5. *In Cases of Abruptio Which Occur During the Course of Gradually Increasing Toxemia, the Location, Appearance, and Consistency of the Blood Clot Indicate That the Initial Bleeding Takes Place at the Site of and Adjoining a Recent Hemorrhagic Infarction of the Placenta (Fig. 6).*—

The maternal blood extravasates first at this point, as shown by the greater indentation and compression of the placenta and the greater firmness and age of the clot at this site. The prognosis for the baby is therefore better if the infarction is nearer the margin of the placenta. (Case 15,42 Fig. 6.)

Kellogg and Hertig[3] are of the opinion that a pathologic process apparently resembling cholesterol-vascular change, affects the intima and lining of the maternal arteries as they reach the placental site and causes spontaneous rupture, extravasation of maternal blood, and abruptio placentae. Reasoning from the

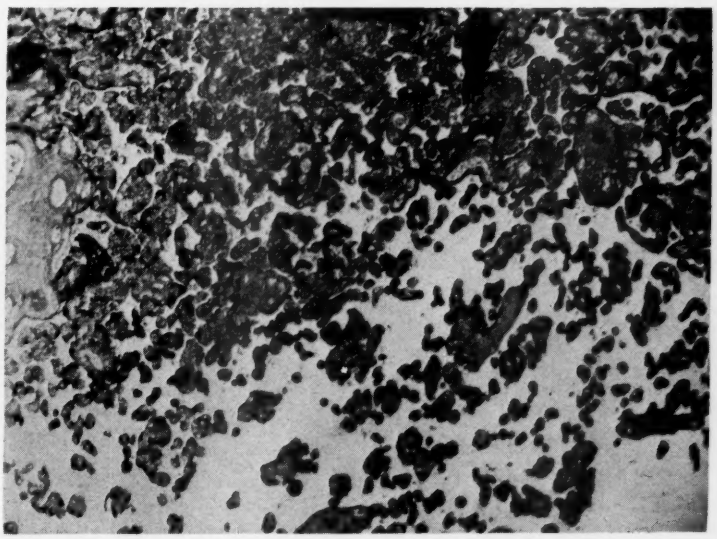

Fig. 4.—Abruptio placentae, Case 43, Fig. 2; low-power magnification at junction of acute hemorrhagic early "E" infarction above, and normal tissue below. The infarcted tissue above shows enlarged, crowded, congested villi; the normal tissue below shows loosely spaced, small, noncongested villi.

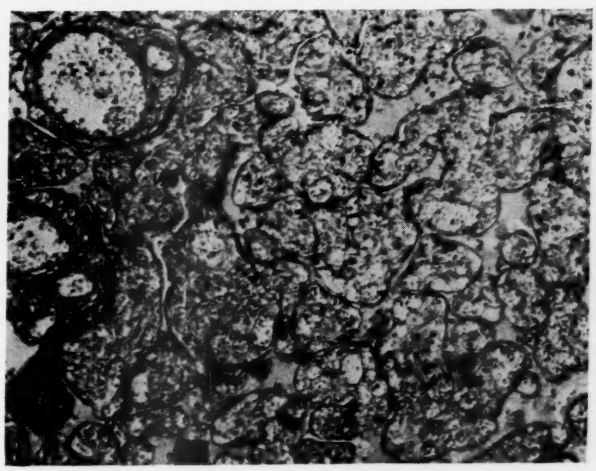

Fig. 5.—Abruptio placentae, Case 43; higher magnification of acute hemorrhagic early "E" infarcted tissue showing enlarged crowded villi, early necrosis and greatly distended villous vessels.

effect of similar change seen in the coronary arteries, it would seem that thrombosis, rather than rupture and hemorrhage, would be the expected result.

The fact that a more advanced stage of necrosis in the infarcted placental tissue, type "D" (Fig. 6), is often seen, indicates an older process than the more recent blood clot adjoining and compressing the infarction and favors

the interpretation that a concentration of the toxic products of placental necrosis (histamine ?) on the adjoining maternal arteries, causes vascular damage, rupture, and hemorrhage.

In fulminating abruptio placentae, the infarction is of the early "E" type and often very extensive, involving one-half to two-thirds of the placenta (Figs. 1, 2). In this case, widespread damage to the underlying maternal arteries takes place, causing extensive extravasation, hemorrhage, and complete separation of the placenta.

In summary, therefore, abruptio placentae should be considered as one of the three possible terminations of true toxemia of pregnancy after reaching the severe or pre-eclamptic stage, namely (1) abruptio placentae, (2) eclampsia, and (3) eclampsism.

Discussion

Despite the pioneer work of Young[4] of Edinburgh in 1914, confirmed by our own investigations of the past fifteen years, also by Hunt, Patterson, and Nicodemus,[5] and in more recent years by Falkiner of the Rotunda,[6] the significance of acute and subacute hemorrhagic placental infarction continues to be questioned or denied. Failure to confirm these findings may possibly be attributed to attempting to cut and interpret the placental strips in the fresh state, rather than in the fixed state by use of ten per cent formalin for several weeks.

Classification, Etiology, and Effects of Placental Infarcts

There are two types of infarcts in the placenta, namely (1) the anemic and (2) the hemorrhagic. The anemic type, "A" and "B" (7, Figs. 1, 3) is undoubtedly due to obliterative endarteritis (8, Fig. 1) which very gradually shuts off fetal circulation to the dependent placental tissue. Slow necrosis of the villi occurs, inducing thrombosis of the intervillous maternal blood, which becomes hyalinized. The villi and their blood vessels are normal in size and are often termed "ghost villi" since they are pale, anemic, and do not stain (8, Figs. 2, 3).

Grossly, the anemic infarct is white, occasionally slightly yellow, and is very firm. It is usually found near the margin of the placenta where the arteries are small and more apt to be obliterated. Slow necrosis minimizes toxic products and the surrounding hyalinized maternal blood precludes dissemination into the maternal circulation. Anemic infarction, therefore, should have no relation to toxemia and this is found to be the case, on comparing the clinical and placental findings.

The acute hemorrhagic infarct, as seen in the formalin-fixed placenta, appears as a dark oval or round area, sharply demarcated from the surrounding normal light-colored placental tissue. The extent of the acute infarction varies all the way from an isolated round or oval area, one to several centimeters in diameter, to an elongated area of infarction, extending through one-third, one-half, or even two-thirds of the width of the placenta. (Figs. 2, 3.) *The isolated and confluent forms* of the infarction take on much significance, as will be seen in discussing the probable cause of the infarction.

The consistency is still soft and spongy as the villi have not yet broken down. For this reason, the lesion does not shine or reflect the light when the strip is held toward the light, horizontally to the line of vision. On bending the entire strip, the infarcted area bends with it.

Microscopically, if one has cut the block to include both the light and dark tissue, the light tissue is seen to be normal, the villi being of normal size,

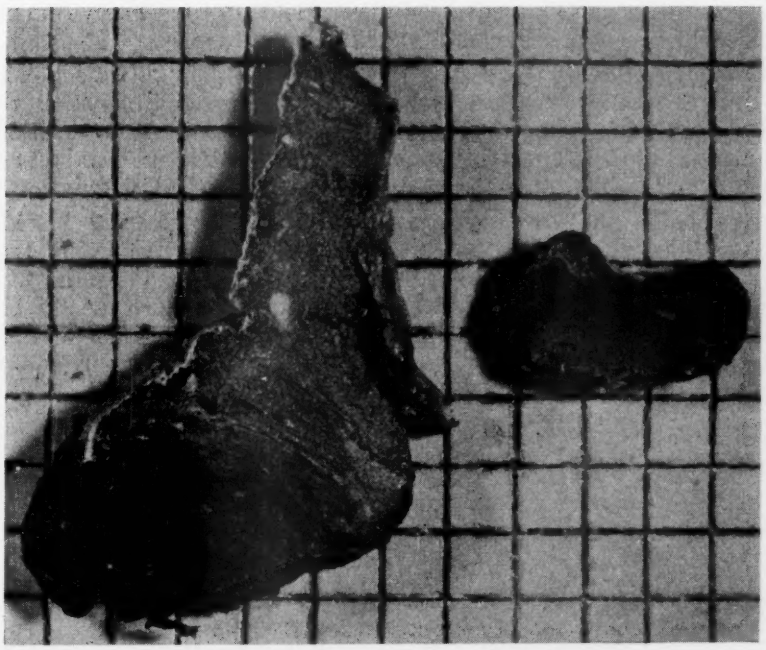

Fig. 6.—Eclampsia and abruptio placentae, Case 42; recent clot adjacent and adherent to underlying older late "E" or "D" hemorrhagic infarction; marginal location of infarction a factor in survival of baby; early "E" hemorrhagic infarction in smaller piece of same placenta probably responsible for simultaneous occurrence of eclampsia.

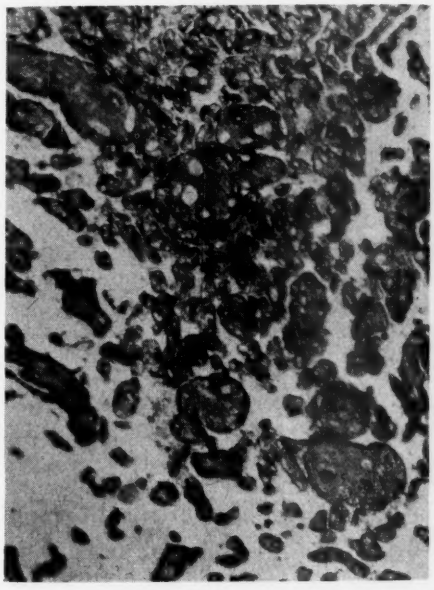

Fig. 7.

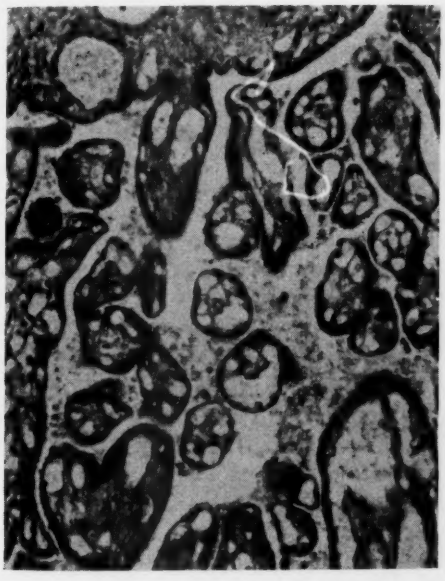

Fig. 8.

Fig. 7.—Eclampsia and abruptio placentae, Case 42; low-power magnification at junction of acute hemorrhagic early "E" infarction above and normal tissue below. Same appearance as in Fig. 4.

Fig. 8.—Eclampsia and abruptio placentae, Case 42; higher magnification of subacute hemorrhagic infarction (late "E" or early "D") showing enlarged crowded villi, more advanced necrosis, and distended villous vessels.

staining well, and spaced loosely over the field (Fig. 4). The villous capillaries and vessels show no engorgement, dilatation, or rupture.

At the line of demarcation the appearance abruptly changes. The villi are of much greater size, crowded, and show early necrosis with pyknosis or karyorrhexis of the nuclei. (Figs. 4, 5.) There is still sufficient intervillous circulation of maternal blood to permit dissemination of poisonous products of necrosis and autolysis of the infarcted tissue through the maternal circulation.

It is probable that histamine is formed from placental histidine at an earlier stage than guanidine, the latter probably resulting from breakdown of placental arginine at a later stage of autolysis. Histamine is productive of vascular damage, shock, and a marked increase in tone of the uterus, all outstanding in abruptio placentae, whereas guanidine may well be the cause of the eclamptic convulsions, since this is known to be one of the characteristic effects. The

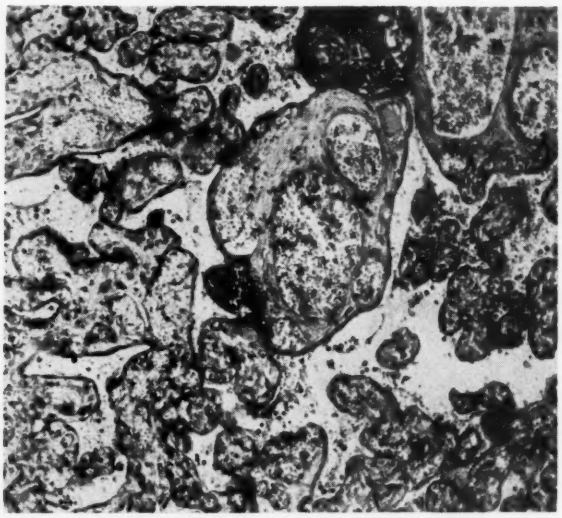

Fig. 9.—Eclampsia, Case 44; higher power magnification of subacute, late "E" hemorrhagic infarction of placenta, showing enlarged crowded villi, necrosis, and greatly distended villous vessels.

capillaries and vessels of the villi in abruptio and eclampsia alike are much distended, engorged, and even ruptured (Figs. 5, 9). Hofbauer[11] produced hemorrhage and placental separation in animals by histamine injections and called attention to the similarity of histamine effects to clinical abruptio.

At a somewhat later stage (subacute) the area of hemorrhagic infarction appears more compact and firm (late "E," Fig. 6) the cut surface being smooth and shiny if held toward the light. On bending the strip of placenta, the area of hemorrhagic infarction, being compact and homogeneous due to fusion of the necrosing elements, does not bend with the strip. It is still dark in color, but if somewhat older, the color change in the hemoglobin imparts a brown color to the lesion, "D" type (Fig. 6).

As to the etiology of the hemorrhagic type of infarction, we formerly attributed the lesion to the trauma of fetal movements on the exposed placental veins, or to the cholesterol vascular change which may be seen microscopically in the lining of many of the fetal vessels. However, thromboses could not be definitely found adjacent to cholesterol deposits in the vessel lining, or at possible sites of trauma on the fetal surface of the placenta, hence these possible factors do not seem to supply the answer.

Spanner's investigations of the placental circulation disclosed certain characteristics of the placental veins which are extremely significant. He demonstrated the *presence of sphincters* in the collecting veins of the placenta as shown in Figs. 10, 11, taken from his publication.[9]

Just what physiological purpose the sphincters serve is not known, but they would seem to insure a more stable content of blood in the villous vessels and to counteract the tendency of uterine contractions to overload the umbilical vein and the fetal heart.

If, however, the sphincters are susceptible to spasmogenic influences originating in pituitary (?) or renal (?) secretions, whether overproduced or insufficiently held in abeyance, the effect upon the dependent villi would be to produce an appearance identical with that which has previously been described in the acute or subacute hemorrhagic infarcts.

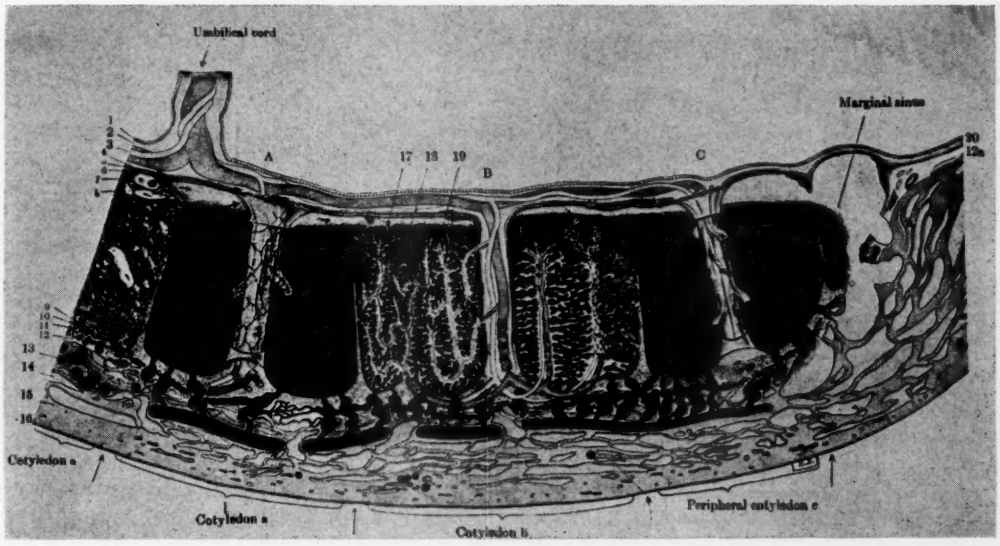

Fig. 10.—Spanner's "Diagram of the Placental Circulation at Term," showing sphincters in main and subsidiary collecting veins of the placenta. Arrangement of veins probably determines form and extent of hemorrhagic infarction (see Figs. 2 and 3). (From DeLee-Greenhill: *Obstetrics.*)

Spasm of the sphincters of the vein serving a unit of placental tissue would at once prevent escape of blood from the unit of dependent villi. The fetal heart, continuing to force blood into this unit through a branch of the umbilical artery, causes the villous vessels to become engorged and distended (Figs. 5, 8, 9). With stoppage of circulation in the vessels, thrombosis follows and the villi become necrotic (Fig. 8). The infarction outlines the pattern of the circulation serving this unit of placental tissue and demarcation is very sharp (Figs. 3, 4). It distinctly places the circulatory disturbance on the fetal and not on the maternal side.

Intrauterine fetal death is followed by maceration of the fetus but is not followed by maceration of the placenta. The cells stain well, the villous vessels show no engorgement or distention, and the villi are of normal size. The inference is that the intervillous maternal circulation is apparently sufficient to preserve temporarily the vitality of the villi and there is no immediate necrosis and toxemia.

However, if there is obstruction to the outflow of blood from the villi through the collecting vein, the resulting distention, engorgement, and thrombo-

sis enlarge and crowd the villi to such an extent that, with maternal intervillous circulation greatly reduced and fetal circulation absent, rapid necrosis results. Toxemia follows dissemination of the poisonous products through the maternal circulation.

As will be noted from Spanner's illustration of the placental circulation (Fig. 10), spasm, affecting the sphincters of a single collecting vein, would affect only the dependent unit of villi, resulting in an isolated, sharply demarcated, oval or round area, appearing very dark on account of the stagnated blood (Fig. 3).

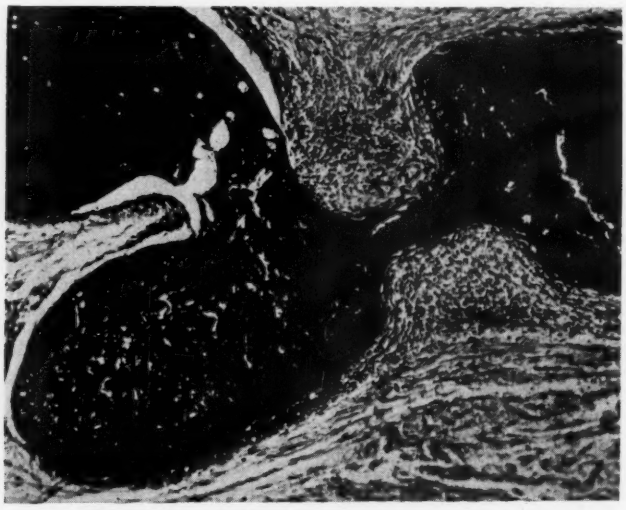

Fig. 11.—Sphincter in placental vein. Low power magnification (Spanner).

If a succession of collecting veins or the main collecting vein, into which the others empty, is involved, there would result a confluent hemorrhagic infarction extending through a considerable area of the placenta (Figs. 2, 3). *The isolated and confluent forms of the infarction are explained by the anatomical arrangement of the collecting veins of the placenta and the appearance is hardly susceptible to any other interpretation.*

Since there is a consistent association of hemorrhagic infarction with acute fulminating as well as subacute toxemia of pregnancy, the arrangement of the collecting veins and the presence of sphincters take on a special significance pointing to the probable sequence of events leading to toxemia of pregnancy.

On this basis, it is also understandable how areas of slight darkening of the placenta might arise from partial or nearly complete closure of the sphincters just before labor, too recent to cause recognizable toxemia, but congesting the veins sufficiently to make an appearance suggestive of a very early acute hemorrhagic infarction. Immediate cutting of the cord at birth and draining away venous congestion might well prevent areas of this suggestive appearance but would not affect true hemorrhagic infarction in which thromboses had already occurred, immobilizing the blood. In the present series, eight placentas were doubtful and four mistakenly diagnosed as toxic through this appearance, or infarction was possibly in the making.

Definite acute hemorrhagic infarction and toxemia may occur after an interval of seven to ten days following the last prenatal visit and cause a patho-

logically positive placenta to be associated with an apparently clinically negative patient. This accounts for an occasional discrepancy in the clinical and pathologic diagnoses on examining "unknown" placentas.

From the foregoing clinical and pathological evidences, it would seem logical to put abruptio placentae in its rightful place as a manifestation of toxemia. Without minimizing the danger from excessive loss of blood in this condition, the associated toxemia has a greater bearing on the mortality and the rationale of treatment than the hemorrhage. One can successfully cope with the loss of blood, but the basic toxemia, with tendency to shock, lessens the patient's ability to withstand trauma and surgical measures.

The time-honored association of placenta previa and abruptio placentae in the textbooks, with the main consideration given to the hemorrhagic aspect of the problems and to surgical treatment, is eminently correct regarding placenta previa but tends to place undue emphasis on surgical interference in abruptio.

It seems more a matter of expediency to recommend cesarean section for severe cases of abruptio placentae found to show little or no dilatation of the cervix at first examination, when it must be admitted, if the same case had been seen for the first time several hours later, the cervix would have shown considerable dilatation and natural delivery would therefore have been recommended (Cases 2, 4, 7, 11, 12, 45, 46, 49).

Miller,[10] by plentiful use of transfusion, was able to show excellent results by cesarean section, but there is reason to believe the same cases would have done equally well with the same blood replacement and natural delivery and future childbearing would not be complicated by a uterine scar. Many cases in our series illustrate this contention.

If there is present that grave but rare disturbance in the blood-coagulating mechanism occasionally found in abruptio placentae, with tendency to uncontrollable bleeding into the tissues as well as from the uterus, it apparently makes very little difference in mortality whether the patient is treated conservatively or by cesarean hysterectomy.[3] Hope for these patients must rest on means of early detection of hemorrhagic tendency. It is admitted in these cases, if serious hemorrhagic tendency can be detected, cesarean section, if resorted to early, may be a lifesaving measure by promptly removing the placental source of the toxin.

If we regard hemorrhagic infarction of the placenta as the source of the toxemia, it does not seem logical merely to control eclamptic convulsions and procrastinate thereafter in terminating the pregnancy. To delay is to permit further damage to vital organs and risk further convulsions through new infarctions.

When abruptio and complete separation of the placenta take place, as evidenced by fetal death, no further absorption of toxins can take place at the placental site. Hence, the mere presence of the fetus and placenta in the uterus should not influence the prognosis. With tendency to limitation of further blood loss by intrauterine pressure, aided if necessary by small and carefully controlled doses of Pitocin to hasten labor, if artificial rupture of the membranes is not quickly effective, and lessening shock and anemia by repeated blood transfusions, we may encourage and await natural delivery.

Simple Classification of True Toxemia of Pregnancy

Finally, it would seem logical to simplify the present classification of the toxemias of pregnancy. One may sense in the opinions expressed in the literature that renal and vascular disease have nothing in common with true toxemia of pregnancy except the associated hypertension. The fact is recognized,

however, particularly with vascular disease, that these conditions do strongly predispose to a superimposed toxemia in the latter months of pregnancy. The high frequency of vascular disease (58 per cent) will be noted in the toxic cases of the above series.

It may well be that the same spasmogenic factor (pituitary and/or renal in origin?) which leads to permanent vascular changes and hypertension, is aggravated by pregnancy (through greater pituitary and/or renal secretion?) and causes greater tendency to spasm of the sphincters of the uterine veins, resulting in superimposed toxemia.

There is some justification for terming pernicious vomiting of pregnancy a toxemia, but it is not on the same basis as true toxemia of pregnancy. Reasoning from the greatly increased incidence of severe vomiting of pregnancy along with the marked increase in chorionic gonadotropin in hydatidiform mole, the effect of this hormone may directly or reflexly give rise to pernicious vomiting. It is probable, however, that toxic effects on the liver and kidneys are rather the result of starvation than of any inherent toxicity of the hormone itself.

Based on the foregoing clinical and pathologic evidences, it would, therefore, seem that there is but one toxemia of pregnancy, namely, that due to autolysis of placental tissue, whether it occurs in acute hemorrhagic infarction of the placenta or by necrosis of avascular hydatidiform villi imbedded at the placental site. The renal and vascular conditions commonly included among the toxemias of pregnancy are, in reality, only predisposing causes.

Is not the term "mild pre-eclampsia" a misnomer? The prefix "pre" certainly implies that eclampsia is about to occur, and if such is the case, neither the symptoms nor the findings can be mild. Many of these cases are vascular disease as shown by the retinal findings and the subsequent mild clinical course. The inference that pre-eclampsia will develop is erroneous, although it is strikingly frequent as seen in our own series.

On the basis of the foregoing evidence, the following would seem to represent the course and classification of true toxemia of pregnancy:

CLASSIFICATION OF TRUE TOXEMIA OF PREGNANCY

SUBACUTE HEMORRHAGIC PLACENTAL INFARCTION (SEVERAL WEEKS)	ACUTE HEMORRHAGIC PLACENTAL INFARCTION (SEVERAL DAYS)
1. Mild toxemia	1. ----------
2. Moderate toxemia	2. ----------
3. Severe toxemia	3. ----------
4. Pre-eclampsia	4. Pre-eclampsia (may not be recognizable)
TERMINATION	
(a) Abruptio placentae or (b) Eclampsia or (c) Eclampsism	

The terminal conditions (a) (b) (c) are listed in the order of frequency. A practical gradation of symptoms and signs from Mild Toxemia to Pre-eclampsia is possible, but will not be detailed at this time.

In the process of autolysis of acute hemorrhagic placental infarcts, it is probable that histamine is produced earlier than guanidine, very much as, in fractional distillation, a certain distillate comes over at a certain temperature, and another at a higher temperature. This may account for a higher incidence of abruptio placentae than eclampsia.

While the opinions expressed in this discussion seem to be dogmatically stated, a sincere endeavor has been made to theorize only to the extent justified by the placental pathology, correlated with the placental circulation and the clinical course. If it should direct thinking and research into paths which to us seem more promising, the effort will be deemed worth while.

Conclusions

1. The frequency with which signs and symptoms of toxemia precede abruptio placentae, the occasional simultaneous occurrence of abruptio and eclampsia, and the identical findings at necropsy, are generally accepted as evidences that abruptio placentae is a manifestation of toxemia.

2. The occasional occurrence of fulminating abruptio without prodromal symptoms or signs of toxemia, has heretofore prevented unqualified acceptance of abruptio as a part of toxemia.

3. The consistent finding of acute and subacute hemorrhagic placental infarction in fulminating abruptio, identical with those found in fulminating eclampsia, plus evidence that the primary site of hemorrhage in abruptio adjoins the site of infarction, furnish additional evidence indicating that abruptio is a part of toxemia of pregnancy.

4. A spasmogenic factor (pituitary and/or renal?) acting on the sphincters of the placental veins probably initiates the following sequence of events: (1) obstruction to the outflow of fetal blood from the dependent unit of placental tissue, (2) distention, thrombosis, or rupture of the villous vessels with resulting enlargement and crowding of villi, (3) diminution of maternal and absence of fetal blood supply to villi from crowding and thrombosis, (4) dissemination of the poisonous products of the resulting placental necrosis with development of symptoms and signs of toxemia.

5. True toxemia of pregnancy of gradual development (several weeks or more) progresses through stages of mild, moderate, severe, and pre-eclamptic toxemia.

6. True toxemia of pregnancy of fulminating development (several days to one week), outstrips characteristic symptoms and signs and reaches the severe or pre-eclamptic stage at once. The lagging symptoms and signs may not appear until the early days of recovery.

7. Severe toxemia or pre-eclampsia terminates in any one of three ways: (a) abruptio placentae, (b) eclampsia, and (c) eclampsism, in this order of frequency. Occasionally (a) and (b) occur simultaneously.

8. Renal and vascular disease are not true toxemias but are predisposing causes, probably through a spasmogenic factor (pituitary and/or renal?) which may cause overaction of the sphincters of the placental veins with resulting acute or subacute hemorrhagic placental infarction and superimposed toxemia.

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Discussion

DR. RALPH A. REIS, Chicago, Ill.—Dr. Bartholomew's solution of the problem of abruptio placentae, eclampsia, and toxemia of pregnancy is intriguing. Careful study of the complete report was both stimulating and provocative for it represents a different approach to an understanding of the etiology, pathology, and course of all three conditions. Dr. Bartholomew and his group find that toxemia of pregnancy frequently precedes abruptio, that abruptio and eclampsia occasionally occur simultaneously, and that abruptio and eclampsia have identical necropsy findings. They consistently find hemorrhagic placental infarcts in fulminating abruptio and fulminating eclampsia and believe that the primary site of the hemorrhage adjoins the site of infarction. They further postulate a spasmogenic factor acting on the placental vein valves, thus producing obstruction to the outflow of fetal blood, followed by distention, thrombosis, necrosis, and rupture of the villous vessels, thereby causing toxemia from the poisonous products of placental necrosis.

In our experience, about 60 per cent of patients with abruptio show toxemia, 8 per cent give a history of trauma, and 32 per cent have neither. Furthermore, the severity of the abruptio does not seem to be proportional to the severity of toxemia. There have been 402 instances of toxemia at Michael Reese Hospital during the past ten years. During the same period there have been 18 instances of eclampsia, none of which had any evidence of abruptio, and 83 cases of abruptio with no evidence of eclampsia. Eclampsia and abruptio do not seem to be as closely linked as the essayists believe. Furthermore, the State of Georgia has five times as much eclampsia (1.56 per cent) as does the State of Illinois (0.31 per cent), but has less abruptio (0.72 per cent) than does Illinois (0.8 per cent). It would seem, therefore, that the majority of toxemias show no evidence of abruptio and that the simultaneous occurrence of abruptio and eclampsia is so uncommon as to be accidental.

The necropsy findings of eclampsia include periportal necrosis of the liver. This is pathognomonic of eclampsia and we have not found these liver changes following abruptio. Neither have we found changes in other organs which could be considered the same for both abruptio and eclampsia. The single exception is glomerulonephrosis of varying degree—a condition which cannot be considered pathognomonic or even characteristic. We have been unable to find hemorrhagic placental infarcts in all cases of abruptio and eclampsia. It is most difficult to differentiate between hemorrhage into the placenta and recent hemorrhagic infarct. The placenta is a highly vascular structure and differentiation is always difficult in richly vascularized tissue. To me, infarction means necrosis of tissue as a result of interference with the blood supply. In many of the slides shown, the normal cell architecture is still present and the cell nuclei seem normal both in configuration and staining reaction. This raises the question as to whether this represents hemorrhage into the placenta rather than hemorrhagic infarcts.

It is difficult to understand how, on the one hand, vein valve spasm can be sufficient to cause distention, followed by thrombosis and necrosis of the villi, thereby causing hemorrhage, abruptio, and toxemia, and, on the other hand, that fetal death leaves the placenta intact and without necrosis because the intervillous maternal circulation is sufficient to keep the villi alive.

Dieckmann believes that the primary pathology of abruptio lies in the maternal vessels of the compact muscle layers of the uterus. Hertig holds that necrosis of the decidua results from acute degeneration of the precapillary arterioles of the placental site. Occasionally toxemia is found with a hydatid mole which has no fetal vessels to thrombose and produce infarcts. Such reports, plus the spread of the hemorrhage through the middle and outer layers of the uterus and the subserosa of other pelvic structures in the Couvelaire type of abruptio placentae, would seem to place the primary pathology on the maternal rather than on the fetal side of the placenta.

More work must be done to clear up these different points of view. Unfortunately, toxemia still remains a "disease of theories."

DR. THADDEUS L. MONTGOMERY, Philadelphia, Pa.—It has been some time since I have had the privilege of discussing a presentation by Dr. Bartholomew on placental pathology. I find much to my amazement that after these several years we are still diametrically opposed in our ideas as to the etiology of placental necrosis and its relationship to eclampsia.

Many of the thoughts that I have had in mind as I have listened to this paper have already been expressed by Dr. Reis but some of them may be emphasized again. The crux of this question which has been raised by the author depends upon whether these lesions of the placenta arise on the fetal side or on the maternal side of the placenta, and whether they precede or follow the toxic manifestations which Dr. Bartholomew has described.

Dr. Bartholomew would have us believe that there are several conditions in the fetal circulation which may be productive of infarction and necrosis of the placenta, and secondary toxemia in the mother. There are many indications to point out that death of the placental villi or life of the placental villi is not dependent upon circulation on the fetal side of the placenta. Prominently among these conditions he has mentioned thrombosis or obliteration of the fetal placental vessels.

However, there are many circumstances which point to the fact that the fetal villi and the chorionic epithelium receive this nourishment from the maternal circulation and are very little dependent on the fetal circulation for their vitality. For instance, after the death in utero of a fetus from some such cause as congenital syphilis, one frequently finds the chorionic epithelium and the villi quite well preserved for 3 or 4 weeks after the fetus has died and all fetal circulation, therefore, has been cut off. However, after premature separation of the placenta, one finds the villi adjacent to the retroplacental clot promptly and immediately degenerated as soon as they are cut off from the oxygen supply in the mother's blood. Also, the findings of hydatidiform mole, as have been mentioned by Dr. Reis, are indicative of the fact that chorionic epithelium is not dependent upon a fetal circulation for its vitality for in this case the chorionic epithelium flourishes, the villi grow rapidly; and yet there is no fetal heart or no fetal circulation to supply these villi with blood from within the villous core.

One may find all of the vessel lesions which Dr. Bartholomew has described at the margin of any normal placenta, where the villi and the villous vessels and fetal vessels have undergone degeneration at their site of attachment to the poorly nourished decidua reflexa.

There are doubtless several mechanisms for the formation of a placental infarct, and certainly one of the most common ones is the formation of an intervillous thrombosis of a local portion of the maternal lake of blood. These recent intervillous thrombi contain red blood cells and are red and firm in consistency. When the red blood cells have undergone autolysis and absorption, a fibrinous mass is left which is gray and firm in consistency. With the first formation of this thrombosis, the villi are cut off from their contact with the oxygen

supply in the mother's blood stream and the individual villi die immediately. Whether or not the intervillous deposit is absorbed in whole or in part, this local portion of placenta is never restored to vitality. The adjacent fetal blood vessels which supply this portion of the placenta naturally collapse; the muscular walls of the arterioles contract, and an atrophic regressive change takes place in the placental circulation at this point. Peculiar to say, a secondary fibrosis or connective tissue development in this area is rarely seen. Possibly the life span of the placenta is too short for such a reaction to take place.

While it is quite true that these areas of intervillous thrombosis and necrosis occur more frequently in the instance of chronic nephritis complicating pregnancy, eclampsia, and other hypertensive states, yet there has never been any evidence to prove that these lesions are the cause of such complications in the mother.

DR. BARTHOLOMEW (Closing).—I want to comment first on Dr. Reis' remarks about the placental tissue not being necrosed.

Regarding the thought that this disturbance is due to interference with maternal rather than fetal circulation, if one will study the lesion at the point where the infarcted tissue borders on the normal, I do not see how one can come to any other conclusion than that the disturbance is fetal. The vessels of the villi are dilated on one side and sharply across the border the villi are entirely normal. If the disturbance came through the maternal circulation there should be no such line of demarcation. If it came through the maternal circulation all of the villi would be affected.

As to Dr. Montgomery's comment questioning why toxemia does not take place very acutely when the fetus dies and the villous circulation ceases, if one examines these placentas after the baby has been dead several weeks he still finds the villi stain well. The vitality of the villi is dependent upon both the fetal and the maternal blood supply. If the maternal supply is cut off by enlargement and crowding of the villi and there is absolute lack of fetal circulation, necrosis takes place. One does not see tissue breakdown when in a state of acute necrosis. The vessels are thrombosed, the nuclei pyknotic, and the tissue does not take a clear stain. The ones that I showed were acutely infarcted. But here is one that is completely fragmented.

In the last few years infarction has been pigeonholed and I do not think we will ever get anywhere in the solution of toxemia unless we include it in the whole question. Vasospasm is an important part of the situation but, to my mind, infarction must be included to furnish the toxic elements responsible for the toxemia.

GYNANDROBLASTOMA OF THE OVARY*

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(From the Washington University School of Medicine, Department of Obstetrics and Gynecology, the St. Louis Maternity Hospital, and Barnes Hospital)

FEMINIZING tumors of the ovary, the granulosal-thecomatous group, may now be considered fairly common tumors of the ovary. Novak[1] states that granulosal-cell carcinoma constitutes about 10 per cent of all the solid malignant tumors of the ovary. The thecomatous tumor is much less frequent. Masculinizing tumors of the ovary on the other hand are rare; a total of about 76 cases have been reported in the literature. A combination of feminizing and masculinizing elements in an ovarian tumor was first described by Robert Meyer[2] in 1930. He coined the term gynandroblastoma for this composite type of ovarian tumor.

A survey of the literature reveals a total of 21 cases described, namely, by Meyer,[2] Tietze,[3] Amati,[4] Schiller,[5] Eerland and Vos,[6] Frankl,[7] Bergstrand,[8] Plate,[9] and Mechler and Black.[10] A critical review of these case reports leaves considerable doubt as to whether several of the tumors meet the criteria for the diagnosis of gynandroblastoma. Mechler and Black likewise have deleted several of these cases on the basis of lack of conformation to histologic and biologic criteria. Schiller[11] has accepted only four of the above mentioned cases for inclusion in this category.

The subsequent case report represents such a lesion. There has been repeated opportunity to study this patient, clinically, pathologically, and endocrinologically, over a period of about two and one-half years. She has already had four laparotomies, three for recurrence of the tumor. There are so many unusual features to this case it seems advisable to report it in some detail.

Case Report

First Hospital Admission.—An 18-year-old, virgin girl entered Barnes Hospital Dec. 8, 1945, with chief complaints of amenorrhea for three years, rapid weight gain, and marked increase in size of abdomen three weeks prior to admission to the hospital. Menarche at age 13, with a regular twenty-eight-day cycle lasting four to five days with moderate flow. After about one and one-half years of a regular cycle, she suddenly became amenorrheic and had not menstruated for three years. She noticed breast development during the time she was menstruating, but on cessaiton of her menses breast development stopped; however, there was no decrease in size. The patient stated, and it was confirmed by her mother, that since onset of amenorrhea she noted her voice had become deeper in pitch; increase and darkening of hair of face, and increased growth of pubic and leg hair. An "electrologist" removed hair on her face one year ago and she had to shave her legs. She had had a pelvic examination by her local physician one year ago and was told she was normal. Psychologically she had a masculine attitude. Her mother stated she preferred to associate and play games with boys rather than associate with girls of her age. Her family and past history were irrelevant. About three weeks before admission she had gained ten pounds in one week. Concomitant with her weight increase, she observed rapid increase in size of her abdomen which she considered

*Presented by invitation, at the seventy-first annual meeting of the American Gynecological Society, Williamsburg, Virginia, May 24 to 26, 1948.

to be fat. About one week before entry in the hospital, she developed a pain in the left lower quadrant. She had no nausea, vomiting, urinary symptoms, nor bowel disturbance. She went to bed because of the pain and after one week she felt well again. She complained of considerable fatigue during this time.

Physical Examination.—Temperature, pulse, respiration, and blood pressure were normal. She had a normal feminine habitus (Fig. 1). There was mild hirsutism of the face, especially of the upper lip and chin (Fig. 2). No chest hair was present. The breasts were small.

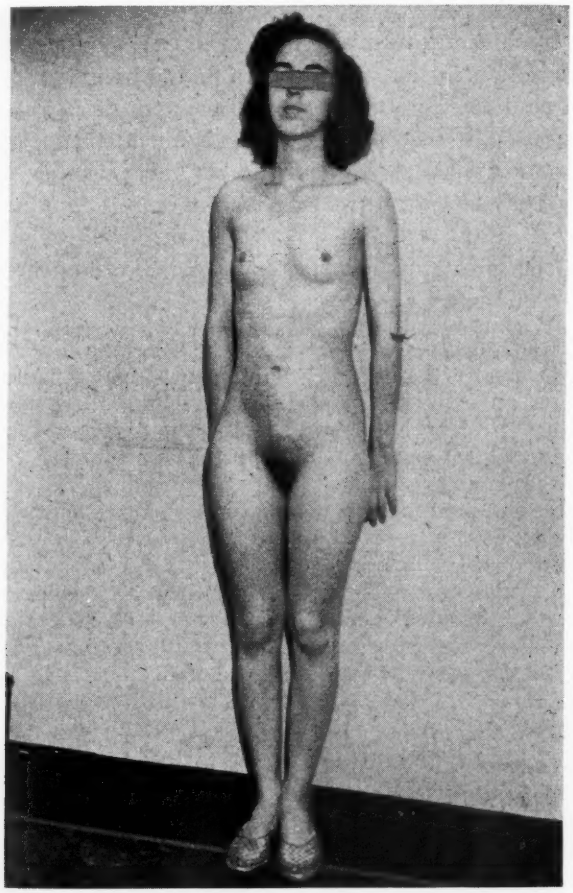

Fig. 1.—Photograph shows normal feminine habitus.

The pubic hair was heavy and dark with mild tendency toward masculine distribution. Heavy growth of hair on the lower extremities was noted. The abdomen was enlarged to the size of a six months' pregnancy. On palpation, a mass could be felt arising from the pelvis which gave one the impression of encysted fluid. A questionable fluid wave was present. No shifting dullness was noted. The abdomen was tympanitic above the mass and dull over it. No sounds were heard over the mass with the stethoscope. No other masses were felt. The liver, kidneys, and spleen were not palpable. Pelvic examination revealed heavy pubic hair, normal external genitals, with the exception of a markedly hypertrophied clitoris (Fig. 3). The hymen was intact. The vagina and cervix were normal to palpation. The

corpus could not be felt but the lower pole of a mass filling the cul-de-sac and extending above the umbilicus was noted. Rectal examination confirmed vaginal palpation. Laboratory data: Urinalysis, negative; blood count: red blood cells 3,540,000, white blood cells 8,050, hemoglobin 11.9 Gm. Differential count was normal. There was slight hypochromasia of the

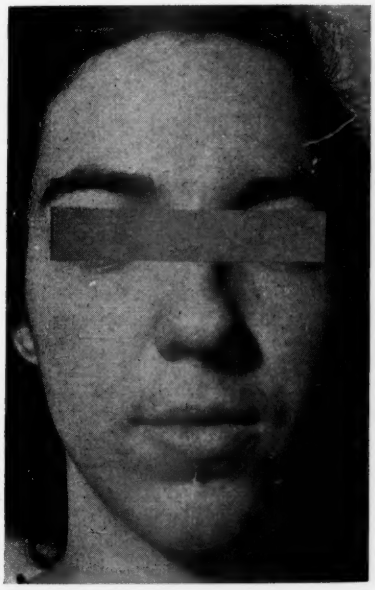

Fig. 2.—Hypertrichosis of upper lip, thick eyebrows, and recession of hair about forehead.

Fig. 3.—Hypertrophy of clitoris.

red blood cells. Platelets appeared adequate. Blood Kahn test negative. Her blood typing was group B, Rh positive. The diagnosis was ovarian cyst, probably a masculinizing tumor with possible torsion of the pedicle. Unfortunately, through a misunderstanding, urine was not collected preoperatively for determination of 17-ketosteroids.

On Dec. 9, 1945, the patient was anesthetized with nitrous oxide and ether. One finger was inserted into the vagina through an intact hymen. The vagina and cervix were normal to palpation. The corpus seemed to be of normal size and forward position. There was a large mass filling the lower abdomen. A small vaginal speculum was inserted and the vaginal mucosa was found to be moderately stimulated. The cervix looked normal. The uterine cavity measured 2½ inches in depth.

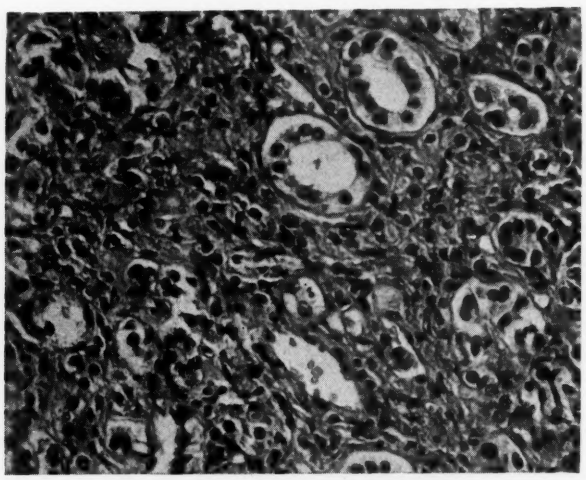

Fig. 4.—Photomicrograph shows tubules and sex cords.

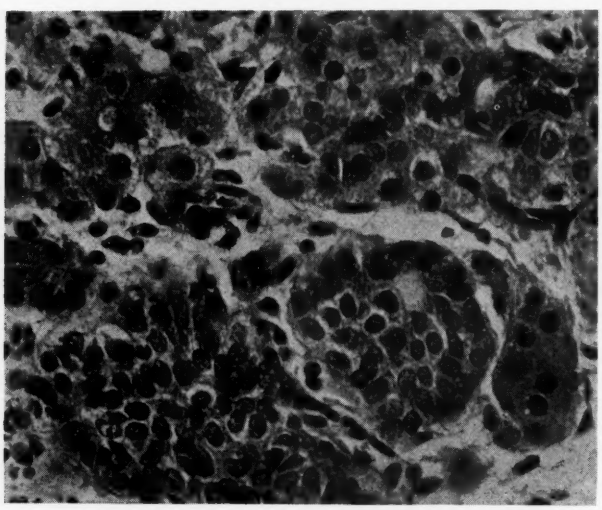

Fig. 5.—Sex cords and islands of interstitial cells are noted.

The patient was then prepared for a laparotomy. When the abdominal cavity was entered, 4,500 c.c. of blood-stained fluid was removed. A large cystic mass the size of a football was found arising from the right ovary. The mass was adherent to the peritoneum anteriorly and posteriorly. The tumor was infiltrated with blood and showed marked

degeneration. While an attempt was being made to free the tumor with the hand, the very necrotic and friable pedicle tore away. Two or three blood vessels in the pedicle were clamped and ligated. The right tube was normal. The uterus, both tubes and left ovary were normal. The left ovary was rather smooth and did not show developing follicles on the surface nor were

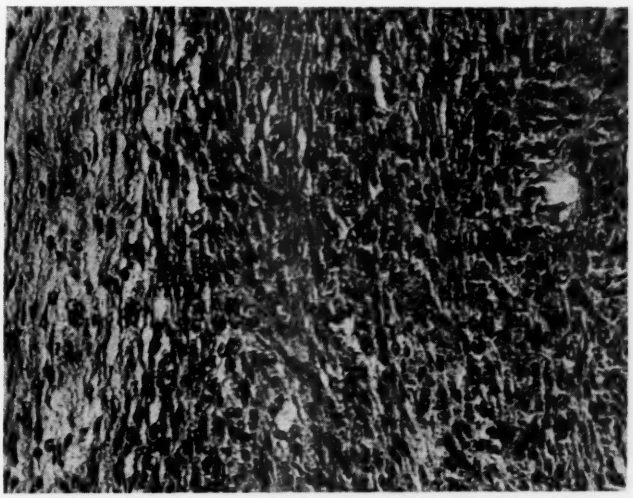

Fig. 6.—Section shows fibromatous character of the bulk of the tumor (femizing portion.)

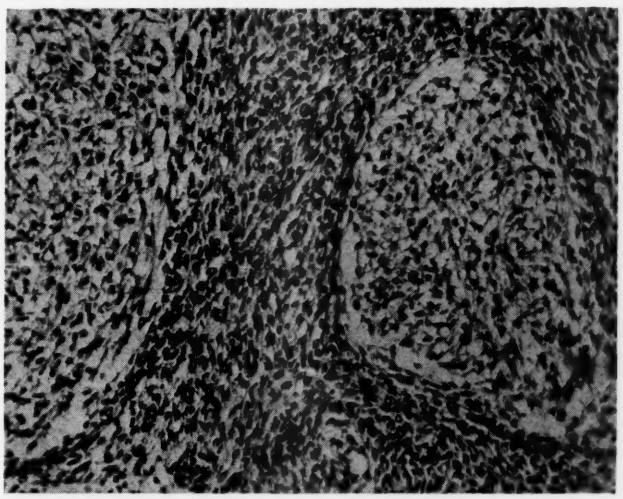

Fig. 7.—Lutein-like transformation of the theca cells.

many stigmata present. Implants on the right parietal peritoneum and in the cul-de-sac were removed. There were no palpable pathologic changes in the upper abdomen. The appendix was removed. During the early phase of removal of the tumor the patient showed signs of shock, drop in blood pressure, rapid pulse, pallor, etc. 500 c.c. blood plasma were given and followed by 500 c.c. of whole blood. The shock rather promptly subsided. The postoperative course was entirely uneventful. On the sixth postoperative day, the patient started to menstruate and flowed for two days. She was discharged from the hospital on the thirteenth postoperative day.

Pathologic Study.—Gross: The tumor consisted of a semisolid mass measuring 18 by 17 by 6 cm. The external surface was roughened, showed hemorrhagic areas with evidence of surface adhesions. There was a broad pedicle which measured 8 by 12 cm. On cut section, the greater part of the tumor was solid but there were multiloculated cystic cavities. Some of the cysts contained a thin hemorrhagic fluid.

Microscopic: Some of the sections showed a definite arrhenoblastoma. In various areas, the characteristic sex cord-like arrangement of the cells was noted, in others, small tubules with a few tubules of rather large size (Fig. 4). There were many clumps of eosinophilic cells which morphologically were characteristic of the interstitial cells of Leydig (Fig. 5). These cells also showed a rich lipoid content. Most sections of the tumor presented the morphologic picture of a diffuse granulosal or thecomatous tumor. This lesion was separate and distinct from the andromatous portion. There was an attempt in some areas at encapsulation (Fig. 6).

Second Hospital Admission.—The patient re-entered the hospital on Aug. 2, 1946, and gave a history of feeling very well since her first operation. Her menstrual cycle was every twenty-eight days and lasted four days. She noticed her breasts were enlarging and hair on her face was disappearing. Her voice was slightly higher pitched. Her mother stated she liked the company of girls now and had become very popular with boys. One month prior to this admission, the patient noted marked enlargement of the abdomen and rapid gain in weight. She experienced some pain in the lower abdomen. Physical examination revealed a rather pale girl in some pain. There was less hair on the face than on the previous admission. Her breasts were slightly larger, too. The heart and lungs were normal. The abdomen was distended by a mass extending almost to the xiphoid. A fluid wave was not perceptible, nor was there shifting dullness. Pelvic examination revealed that the clitoris had not decreased in size. One-finger examination of vagina showed the vagina and cervix normal to palpation. The vaginal mucous membrane appeared well stimulated. None of the pelvic structures could be palpated. Rectal examination was not revealing. A paracentesis was done with removal of 30 c.c. of bloody fluid. The sediment was examined for malignant cells but none was found. An x-ray plate of the chest showed normal cardiac silhouette, hilar shadows and lung markings. Both leaves of the diaphragm were high. Laboratory studies: Urinalysis showed no abnormalities. Blood count: red blood cells 3,690,000; hemoglobin 11.9 Gm.; white blood cells 9,300; with a normal differential count. Twenty-four-hour urine specimen showed no detectable steroid glucuronidate and 4 mg. of 17-ketosteroids. The preoperative diagnosis was either recurrence of the gynandroblastoma or a new tumor involving the left ovary.

A laparotomy was performed on Aug. 8, 1946, and 2,500 c.c. of bloody fluid was removed. On palpation, there was a very large mass extending from the pelvis to the xiphoid process. The mass was attached to the posterior surface of the uterus, broad ligaments, parietal peritoneum, omentum, and intestines. The tissue was friable, cystic, and contained bloody fluid. The mass was scooped out by the handful, enough to fill a large basin. The neoplasm did not infiltrate the tissue but was adherent to the surface and could be wiped and peeled off. The left ovary, both tubes, and the uterus were normal. Since it was decided to give the patient deep x-ray therapy, it seemed advisable to remove the left ovary for study. At the end of the operation, all of the visible neoplastic itssue was removed cleanly. Gelfoam was used in the cul-de-sac to control oozing. Immediately after the removal of the neoplastic growth was started, the patient went into profound shock, with imperceptible pulse and blood pressure for fifteen minutes. She was given 1,000 c.c. of citrated blood and soon her condition gradually improved. Her postoperative course was uneventful and she was discharged from the hospital on the twenty-third postoperative day. She received 500 c.c. of whole blood on the seventh postoperative day to correct her anemia. Deep x-ray therapy was started on the eleventh postoperative day and was continued with the patient ambulatory after discharge from the hospital. In a period of thirty-one consecutive days, a total of 8,200 r. was given over eight portals, four anteriorly and four posteriorly.

Pathologic Study.—Gross: The specimen consisted of 1.3 kg. of cystic, necrotic tissue. The largest piece of tissue measured 13 by 11 by 2 cm. Most of the cysts were ruptured

but a few small ones contained a clear brown fluid. The left ovary measured 5 by 3½ by 2½ cm. On cut section, the ovary showed normal architecture with a recent corpus luteum and several developing follicles.

Microscopic: Sections of the tumor showed fibromatous, epithelioid type of cells growing diffusely. Morphologically, the cells were of the diffuse granulosal-thecomatous type. There was marked vascularity and extravasation of blood into the tissue. Multiple sections failed to show any andromatous structures. Sections of the left ovary revealed normal histology.

Third Hospital Admission.—The patient again entered the hospital on Sept. 3, 1947, and had had no complaints until two weeks previously, at which time she noted pain and swelling of her abdomen. Patient gained ten pounds in two weeks. Physical examination revealed a normal woman with the exception of a mass filling the abdomen to the level of the umbilicus. Pelvic examination showed no change in the size of the clitoris from the first examination. The vaginal mucosa looked fairly well stimulated. On rectal examination, a mass filling the lower abdomen was palpated. Chest plate was negative. Laboratory data: urinalysis was negative; blood count: red blood cells 4,150,000, hemoglobin 10.8 Gm., white blood cells 10,300. Differential count was normal. Blood nonprotein nitrogen was 17 mg. per cent. Blood sugar was 59 mg. per cent. Total protein was 6.2 Gm. per cent; albumin was 3.8 Gm. per cent and globulin 2.4 Gm. per cent. Blood Kahn test was negative. Twenty-four-hour urine specimen showed 7 mg. steroid glucuronidate and 9 mg. .17-ketosteroids. The preoperative diagnosis was recurrent gynadroblastoma of the peritoneum.

A laparotomy was done on Sept. 5, 1947. When the abdominal cavity was entered, approximately 8 L. of straw-colored fluid were removed. A large amount of friable tissue which contained fluid and blood was attached to the parietal peritoneum, serosa of the intestines, under surface of the liver, and a large mass 10 by 10 cm. was attached in the cul-de-sac and adherent to the posterior surface of the uterus and broad ligaments. The tissue was so friable that it was scooped out with the hand. Again, the neoplastic tissue was loosely attached to the liver, intestines, and parietal peritoneum. All gross tissue was removed, with the exception of a small area in the cul-de-sac. The uterus was normal in size. The right tube was removed. There was no evidence of metastases into the liver. The intestines were free and the parietal peritoneum clean at the end of operation. Again, the patient showed the same picture of shock as soon as the abdomen was entered as on the two previous operations. The patient recovered from her shock upon the administration of whole blood. The postoperative course was uneventful with the exception of moderate anemia which was corrected by whole blood transfusion. She was discharged on the fifteenth postoperative day.

She again received deep x-ray therapy as an ambulatory case for a consecutive period of nineteen days for a total of 6,400 r. over the abdomen and back.

Pathologic Study.—Gross: A large amount of friable hemorrhagic tumor tissue consisting in part of numerous small pieces to which were attached pieces of omentum and fragments of peritoneum; another part consisted of a rounded solid mass of tissue measuring 10 cm. in diameter. On section of this tissue there was hemorrhage giving it a mottled appearance. The tissue had a brain-like consistency. A few small cavitations were present which contained old blood or mucoid material.

Microscopic: Multiple sections of the tissue revealed only the thecomatous type of cells. No andromatous elements were found. In one area there was lutein-like transformation of the cells (Fig. 7).

Fourth Hospital Admission.—On Jan. 14, 1948, the patient stated that she had never felt better in her life until twenty days previously. At this time she noted rapid enlargement of the abdomen. She had some anorexia, nausea, and vomiting. Physical examination revealed a thin female with a markedly protruberant abdomen. All of the positive findings were confined to the lower abdomen. A large mass could be palpated. A fluid wave was present. The vaginal mucous membrane appeared fairly well stimuated. Rectal examination revealed a large mass filling the lower abdomen. Chest film was negative. Laboratory data: Urinalysis was negative. Blood count: Red blood cells 3,690,000; hemoglobin 11.1 Gm.; white blood

cells 6,910 with normal differential. Carbon dioxide capacity 68.5 volumes per cent, or 31.1 mg. per L. equivalent; chlorides 376 mg. per cent equivalent to 160 mg. per L. Twenty-four-hour urine specimen showed 9 mg. pregnanediol glucuronidate and 2 mg. 17-ketosteroids. The preoperative diagnosis was recurrence of gynandroblastoma.

A laparotomy was done on Jan. 15, 1948. When the abdominal cavity was entered 3 L. of ascitic fluid were removed. There was a large amout of degenerated tumor attached to the parietal peritoneum, intestines, and especially a large amount attached to the under-surface of the liver. Again, the tissue did not infiltrate the organs but adhered to the surfaces. There was very little tumor found in the pelvis. All of the gross tissue was again scooped out and wiped off the organs. A small amount of the neoplasm could not be removed from the under surface of the liver. Considerable oozing from the liver was controlled by topical thrombin and packing. Again, the patient exhibited the same pattern of shock as in the three previous operations. She rallied from her shock on the administration of 1,500 c.c. of whole blood. Her postoperative course was complicated by some abdominal distention, nausea, and vomiting. On her eleventh postoperative day, deep x-ray therapy was again started. She was given 8,000 r. over a period of thirty-five consecutive days. This time therapy was given over both flanks and upper quadrants in addition to the usual portals over the lower abdomen and back. She was discharged from the hospital on the thirty-second postoperative day. Her long hospital residence was due to the fact that the x-ray department wanted her under close observation during the first part of her treatment. The patient has no complaints at the present time and has gained considerable weight. She stated specifically that she has never had a hot or cold flash.

Pathologic Study.—Gross: The specimen consisted of a large amount of hemorrhagic fragmented neoplastic tissue. The largest piece measured 8 by 6 by 4 cm.

Microscopic: Many sections failed to show any epithelial structures. Only thecomatous pattern was present. Again, areas of luteinization were noted.

Discussion

This case presents the usual clinical-pathologic picture of an intermediate type of arrhenoblastoma. In addition, it exhibits histologic and biologic evidence of an estrogen-producing tumor. The histogenesis of gynandroblastoma is of considerable interest. The masculinizing portion of the tumor may arise, as pointed out by Meyer in cases of arrhenoblastoma, from male-directed cells persisting in the ovary from early development; the feminizing portion may originate from remnants of granulosal cells left over in the process of follicle formation. In other words, it is theoretically possible for two tumors of different structures to develop in the same ovary. This seems to be the most likely origin in this case. The absence of intermingling of the andromatous and feminizing portions would point to this conclusion. Robert Meyer[2] suggests an origin from indifferent cells which may functionally and morphologically become hermaphroditic, so that both androgens and estrogens may be elaborated. Mechler and Black[10] suggest a teratomatous origin.

It is of interest that this patient has never had symptoms of castration with the exception of amenorrhea. She has never had vasomotor symptoms, headaches, nervousness, nor depression which is usually associated with castration in a young woman. Her vaginal mucosa has appeared well stimulated at all times. This has only one implication and that is the tumor tissue is elaborating estrogens. An endometrial biopsy has not been obtained because at each opera-

tion her condition has been too precarious to permit it. It would be impossible to get such a biopsy without anesthetizing the patient. A recent vaginal smear showed exfoliation found in women with mild estrogenic stimulation.

The age of patients in the reported cases has ranged from 17 to 76 years. Only one other patient was younger than this one. Most of the tumors have been relatively small. This one was very large.

No case of gynandroblastoma reported had had so many repeated endocrinologic and pathologic studies. The patient exhibited the classical picture of acquired virilism; hirsutism; enlargement of the clitoris and amenorrhea, yet there was no increase in the 17-ketosteroids or the steroid glucuronidate in the urine. All of the urine specimens obtained were secured, of course, when there was a large amount of active tumor tissue growing in the abdominal cavity. The failure to find increased amounts of steroids in the urine does not indicate that unusual amounts of androgens were not being elaborated by the tumor. For example, Geist and his co-workers[12] have shown that 500 mg. of testosterone per month is sufficient to induce virilism in normal women, yet this amount would increase the daily excretion of ketosteroids by only a few milligrams at the most.

The sequence of events in this patient is such that the tumor must have been elaborating steroids, presumably androgens, or possibly progesterone, and estrogens which induced the amenorrhea by inhibition of the anterior pituitary. Then, following the removal of the tumor, the pituitary recovered its normal activity and normal cycles were resumed. The fact that the patient started her menses six days after removal of the tumor is prima facie evidence that the bleeding was due to deprivation of estrogen or possibly progesterone. It was evident that endometrium was already stimulated by sex hormones elaborated by the tumor. In virilizing tumors, either adrenal or ovarian, the pituitary usually does not recover for one to two months. But despite recurrence of the tumor normal cycles persisted to the time of removal of the other ovary, indicating that the recurrent tumor had biologic characteristics different from the original tumor. Histopathologic study also shows that the recurrent tumor lacks the masculine elements found in the original new growth.

The tumor has grown in a peculiar manner. It has propagated on the surface of the organs. It is always amazing to see how clean the abdomen is after removal of the tumor. Numerous operations are anticipated unless the tumor takes on a different method of propagation.

There has been unusual opportunity to study the effect of deep x-ray therapy on the tumor. Although she has had a total of 22,600 r. over a period of a little less than two years, there has been slight evidence of regression such as pyknotic nuclei, vacuolization of cells, and edema. The greatest suggestion of benefit has been the relatively little tissue found in the pelvis on the last two operations as compared to the increased amount in the upper abdomen. Perhaps the explanation for this is the fact that most of the therapy has been concentrated in the pelvic region.

Summary

A young girl, 18 years old, has both a feminizing and virilizing tumor of the same ovary from a morphologic standpoint. The clinical features of this case suggest a combination of the hormonal effects of androgens and estrogens. The antagonism of these two hormones is complex. The primary tumor showed a predominance of androgens from a biologic consideration since there was defeminization and masculinization. After removal of the tumor, even though it has repeatedly recurred, there has been no biologic or histologic evidence of androgen elaboration, while, on the other hand, there has been clinical evidence of estrogen production. A study of 17-ketosteroid excretion in this case has not been of clinical value. Roentgen-ray therapy undoubtedly has an effect on slowing the tumor growth but apparently is not lethal to the cells, even in large concentration. This tumor histologically lacks most of the criteria for malignancy yet it is recurrent and locally invasive.

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Discussion

DR. J. P. PRATT, Detroit, Mich.—The unusual clinical picture just presented by Dr. Hobbs invites speculation as to the genesis of mixed tumors of the ovary. Since he has confined his report mostly to the clinical features, the discussion may well follow the same direction. I have not had a similar experience but it has been my privilage to review the microscopic sections from a case reported by Dr. Christopher of Detroit. His report is now in press and he has generously offered to let me use some of his data. He, as well as Mechler and Black, has carefully reviewed the pertinent literature.

The name *Gynandroblastoma* was first suggested by Robert Meyer in 1930 when he presented to the Berlin Gynecological Society a series of arrhenoblastomas. One of his tumors contained elements similar to granulosa-cell tumors. The uterus was hypertrophied.

Plate, in 1938, reported a tumor showing both granulosa cell and arrhenoblastoma and he collected twelve cases from the literature which he believed could be classified histogenetically and morphologically as a combined tumor.

Mechler and Black, in 1943, reported a case of gynandroblastoma and reviewed the literature. Schiller, in a discussion of this paper, accepted only four cases of gynandroblastoma (Plate, Frankl, Schiller, Mechler and Black), and later accepted Christopher's case. Robert Meyer accepted the diagnosis of granulosa cell in Christopher's case but was not so sure of the arrhenoblastoma elements.

Christopher's patient, aged 28 years, was first seen in March, 1936. She complained of lower abdominal pain for 30 days and menorrhagia for 11 months. Menstruation began at age 14 and was regular every twenty-eight days until she bore her first child in 1927. Delivery of this child was followed by amenorrhea for nine months. Following the birth of the second child in 1929, she had menorrhagia and metrorrhagia, her voice became deeper, and libido decreased. She had a deep voice, scant hirsutism, and mild hypertrophy of the clitoris. The breasts were small and flat. At operation, a tumor of the right ovary, the size of a lemon, was removed. The left ovary was small and fibrous. The uterus was uniformly hypertrophied. (No hormone studies were done). Following operation, vaginal bleeding ceased and a normal menstrual period occurred three months after operation. Menstruation has been normal since (12 years). Her voice remained deep, the clitoris remained enlarged, the breasts enlarged and the libido increased. Curettings taken at the time the tumor was removed showed a post-menstrual endometrium corresponding to the eighth day of the cycle.

All but one of the tumors reported were unilateral and most of them were benign. Although the six cases reported are not alike, it would seem that there are enough points of similarity to justify a tentative preoperative diagnosis of gynandroblastoma when certain conditions are fulfilled. An ovarian tumor associated with evidence of masculinization and hyperestrinism is suggestive. Endocrine assays may be indicative in some future case, but in the previous reports the procedure has not helped the diagnosis. No constant pattern in the tumors has been reported but all showed some combination of granulosa cell and arrhenoblastoma. Since the macroscopic appearance of arrhenoblastoma and granulosa-cell tumors is similar, the clinical history should suggest a more diligent search microscopically for the combined elements of tumors.

Why has virilism been diagnosed by clinical manifestations but not by hormonal assays? Androgens are capable of inhibiting menstruation in normal women by inhibiting pituitary secretion of gonadotropins, thereby removing the stimulus to ovarian activity. Granulosa-cell tumors apparently produce estrogens, independent of pituitary influence. The influence of androgens in all six cases produced virilism and in three cases, amenorrhea. In one report, the menstrual history was not recorded. Clinical evidence will depend upon the amount of androgens and estrogens, antagonism between the hormones and the ability of the receptor to respond to the hormones. Besides amenorrhea, the most conspicuous symptoms of virilism were hirsutism, low-pitched voice, and hypertrophied clitoris.

It is remarkable how long increasing signs of masculinization are tolerated by the patient before seeking medical attention. (Dr. Hobbs' patient waited three years, Dr. Christopher's seven years). During that time, the anatomic structures were changing and when masculinization once becomes established, it is irreversible. The transition is so gradual that no sign or event is conspicuous to the patient or her family.

We are fortunate to have had our attention directed to this unusual ovarian tumor. This presentation should be a stimulus to us to look more carefully for clinical and pathologic evidence of gynandroblastoma.

DR. LUDWIG A. EMGE, San Francisco, Calif.—No typical gynandroblastoma has come to our attention though we have seen tumors of the ovary harboring components of both male and female gonadal derivatives. We have classed these as mesenchymomas for want of a better term simply to indicate their period of formation as lying somewhere between dysgerminoma and well-differentiated functional tumors of unilateral sex development. Such a tumor was recently reported by Dr. Albert Long, in *California Medicine*. The respective patient consulted us for rapidly increasing hirsutism accompanied by hemothorax similar to Meigs' syndrome. The tumor revealed a preponderance of granulosa-cell elements and dispersed androgenic components. The endometrium presented a typical hyperplasia. All symptoms disappeared with the elimination of the tumor with the exception of the hirsutism. 17-ketosteroids leveled off from 21.3 mg. in twenty-four hours before operation to 16 mg. twenty months later. It is difficult to explain the persistence of hirsutism unless it occurred independently from the androgenic factor in the tumor. The fact that the 17-ketosteroids remained close to the upper limit of the average normal hints at an adrenal factor.

Dr. Hobbs stated that the ketosteroid factors obtained in connection with his case were normal. Unfortunately no readings were taken except immediately after surgery when 17-ketosteroids are notoriously low. Besides, the average normal varies for a given method of purification. For instance, in our laboratory, the average normal was found to vary from 5 to 18 mg. in 24 hours, while Hamblen and Talbot give 4 to 5 mg. and Pincus and Friedgood 9 mg. The same holds good for pregnandiol determinations. If Dr. Hobbs had taken these factors into consideration, more might have been learned about the functional significance of his tumor in relation to the symptoms presented. Failure to obtain endometrium for a similar purpose was a regrettable oversight since the endometrium at least might have given a hint as to the functional preponderance of either component of the tumor described. While the case presented by Dr. Hobbs is most interesting, I believe that more basic information of real value could have been added to our still fragmentary knowledge of functional tumors by a more exhaustive endocrine study.

DR. CHARLES A. BEHNEY, Philadelphia, Pa.—The subject of this presentation, a most unusual combination of two neoplasms, one extremely rare, with bisexual characteristics, afforded an opportunity to observe the physiology and chemistry of a tumor. We have never encountered growths of this type nor are we aware of any having been found in the Philadelphia area.

In retrospect, it is regrettable that certain studies were omitted for one reason or another. Information provided by complete hormonal assays, vaginal spreads, endometrial biopsy, the basal metabolic rate, glucose tolerance test, and x-ray examination of the skull might have disclosed some interesting and helpful data. Investigation of the adrenals by intravenous pyelogram, costovertebral insufflation, the chloride excretion test, and palpation also appear to have been indicated.

If the condition of the patient after laparotomy precluded curettage, endometrial biopsies might have been secured preliminary to the major procedure or during the intervals between operations. In view of the frequent association of fundal cancer with granulosa-cell tumors a curettage should still be done. The additional hazard, if any, involved by hysterectomy, rather than appendectomy on one occasion or oophorectomy on another, would have been justified.

This tumor appears to have behaved very much as in a tissue culture, thriving here and there until the nutritional capacity of the environment of the transplant was exhausted, and then becoming necrotic. The lack of evidence of invasiveness or metastases makes the propriety of malignant classification as questionable as in the case of a pseudomucinous cyst or an endometrioma, both of which can be transplanted and do recur.

DR. HOBBS (Closing).—I quite agree with Dr. Emge that further hormonal studies should be done and that is my intention. To be sure, the value of 17-ketosteroids will vary in different laboratories. Compared to the normal established in our laboratory, this patient had a low normal value. These hormonal studies were of no differential significance in this patient.

Dr. Behney has made some excellent suggestions for further study of this patient. Several of these procedures have already been done. Unfortunately, an endometrial biopsy cannot be done without anesthetizing the patient. At the next operation I intend to do an endometrial biopsy first. More frequent study of vaginal smears may be of value in evaluating the estrogenic activity.

THE PHYSIOPATHOLOGY OF ECLAMPSIA*

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DURING nine months of 1945, five women suffering from pregnancy toxemia died on our service at Parkland Hospital. Tables I and II. This represented the mortality experience with toxemia during two years. Since then, a mildly toxemic patient died with proved pleurisy of hemolytic staphylococcus origin. After careful review of the case histories, it was at once evident that pulmonary edema accounted for four of the five deaths and was a feature in the fifth. Treatment philosophy, at the time, was concerned with efforts to overcome oliguria by copious intravenous injections of normal and hypertonic fluids. Cessation of this practice brought gratifying results. There has been no death from, or associated with, pregnancy toxemia at Parkland Hospital since October 28, 1946. Moreover, pulmonary edema has not been observed since. No other change was instituted in the treatment of either convulsive or nonconvulsive toxemia, and it remains ultraconservative. The experience with convulsive toxemia during 1946, 1947, and the first trimester of 1948 is given in Table III.

TABLE I. TOXEMIA* STATISTICS, PARKLAND HOSPITAL, 1944, 1945, 1946, 1947, 1948
(FIRST TRIMESTER)

Patients discharged	8,090	
Patients delivered	6,555	
Toxemic patients, total	520	
Convulsive toxemia		34
Nonconvulsive toxemia		486

*Toxemia was diagnosed when a pregnant woman exhibited two of the following signs: hypertension, albuminuria, edema.

TABLE II. DEATHS FROM TOXEMIA OF PREGNANCY, PARKLAND HOSPITAL

	NUMBER OF DEATHS*						
	1944	1945	1946	1947	1948 FIRST TRIMESTER	TOTAL NUMBER	TOTAL PER CENT
Convulsive toxemia (34 patients)	0	3	0	0	0	3	8.3
Nonconvulsive toxemia (486 patients)	0	2	1	0	0	3	0.6
Total (520 patients)	0	5	1	0	0	6	1.2

*Note that most of the fatalities (five-sixths) occurred in 1945.

*Read at the seventy-first annual meeting of the American Gynecological Society, Williamsburg, Virginia, May 24 to 26, 1948.

TABLE III. ECLAMPSIA,* PARKLAND HOSPITAL

AGE	PARITY	CONVULSIONS		MORPHINE (GRAINS)	INFANT FATE
		ONSET	NUMBER		
		1946			
32	5	Antepartum	1	0.75	Alive
15	0	Antepartum	3	1.25	Alive
18	0	Antepartum	9	0.80	Alive
40	0	Postpartum	2	0.50	Alive
22	0	Intrapartum	1	2.25	Alive
35	4	Postpartum	4	2.00	Triplets—Alive
19	3	Intrapartum	3	2.00	Alive
20	0	Intrapartum	1	0.75	Alive
14	0	Intrapartum	2	2.75	Alive
19	0	Intrapartum	1	3.75	Alive†
		1947			
18	0	Antepartum	9	3.25	Dead
17	0	Antepartum	1	2.13	Alive
19	0	Antepartum	2	5.00	Alive‡
28	1	Postpartum	1	1.16	Alive
22	0	Postpartum	1	0.50	Alive
13	0	Postpartum	2	2.25	Alive
22	0	Antepartum	1	1.63	Dead
16	0	Antepartum	10	4.50	Dead
19	0	Intrapartum	1	0.75	Dead
15	0	Antepartum	3	2.50	Dead
26	1	Antepartum	5	2.00	Dead
		1948, First Trimester			
15	0	Intrapartum	1	0.50	Twins—Alive
16	0	Antepartum	3	0.50	Alive

*There was no maternal death in this consecutive series of 23 women with convulsive toxemia.

†This infant survived the intrapartum administration of 3.75 grains of morphine sulfate.

‡This infant survived the antepartum administration of 5.00 grains of morphine sulfate.

Note.—Since preparation of these data, another patient recovered. Her child also survived. The Fetal Mortality Rate is, therefore, 22.2 per cent, (21 living children; 6 dead).

There was no maternal death in this consecutive series of 23 women.* Twenty-six children were born to these 23 mothers, including a set each of triplets and twins. There were six fetal deaths, 23.0 per cent, or a 77.0 per cent survival rate, despite the employment of heavy doses of morphine sulfate. Even if the fortuitous circumstance of survival of all the infants of the multiple births is discounted, the death rate of six children from 23 births would be only 26.1 per cent. For the sake of completeness, details concerning the six fetal deaths are given in Table IV. Parkland Hospital serves the indigent population of Dallas. Half of our clientele is Negro, one quarter is Mexican, and there is no opportunity for selection of patients. Nearly one-fourth of the patients appear for the first time in labor, many of the remainder come infrequently to prenatal clinic, and we count ourselves fortunate to see them more than once before term. Obviously, we cannot continue to manage pregnancy toxemia under such conditions without maternal fatality.

The current treatment for convulsive toxemia at Parkland Hospital is summarized below. Upon admission, or after the initial convulsion, ¼ grain of morphine sulfate is injected intravenously and ¼ grain subcutaneously. Addi-

*Since then, another patient recovered from convulsive toxemia. Survival of her child reduces the infant mortality rate to 22.2 per cent.

tional drug is administered (with 30 minutes between treatments for time to observe effect) in order to reduce the respiratory rate below 14, but not below 10 per minute. Occasionally, an enema of 200 c.c. of tap water containing 20 or 30 grains of chloral hydrate is substituted to avoid excessive morphinization. External stimulus, such as bright light, noise, needle pricks, and catheterization, is avoided. A medical student remains in constant attendance. *Fluid intake is limited to replacement of the daily insensible loss* (assessed at 1,500 c.c.) plus an amount equivalent to the urinary excretion of the previous twenty-four hours. This is not dehydration treatment; rather it is a policy of maintenance of fluid balance. Five per cent dextrose in distilled water is the standard infusion medium, and no hypertonic solution or plasma is employed. The obstetric status is ignored during the convulsive phase and treatment conducted without regard for the pregnancy. After convulsions are controlled and the patient becomes conscious, sedation is achieved with phenobarbital. The patient remains absolutely in bed, and generally accepted dietary principles, including high protein and low salt content, are followed. Labor is induced by rupture of the bag of waters two, or preferably three, days after the last convulsion. No ancillary treatment is employed, and operative delivery is performed only upon obstetric indication.

TABLE IV. FETAL DEATHS*

NAME	BIRTH WEIGHT (GM.)	CAUSE OF DEATH
M. F. B.	2,806	Macerated stillbirth
M. S.	1,587	Macerated stillbirth
S. T.	1,602	Born alive. Died shortly
J. J.	4,270	Born alive. Died 19 minutes later. Cause unknown
C. W.	1,588	Born alive. Died next day
E. C.	1,587	Born alive. Died shortly

*Note that only one fetal death, the infant of Mrs. J. J., can be attributed to factors relating to labor.

Discussion

It seems that avoidance of excess injection of fluid improved our toxemia recovery rate. If this is true, and not the result of chance, why are toxemic patients sensitive to fluid overload? Arteriolar spasm provides a satisfying answer to the question. There is irritability, but no resiliency of the muscular walls of the arterioles, with marked decrease of ability to accommodate fluid injected into the vascular tree. Moreover, the rate of water excretion by the kidney is seriously curtailed as a result of glomerular ischemia. These combine to make the toxemic woman resistant to sudden increase of blood volume. Right heart failure with pulmonary edema can, therefore, follow injection of a much smaller volume of fluid than is the case with a normal individual. Whether or not this is the correct explanation, these facts cannot be denied: 1. Pulmonary edema accounted for the deaths of four toxemic women and was a feature in the death of a fifth. 2. Since we adopted a policy of simple maintenance of fluid balance, no toxemic patient has died and none has developed recognizable pulmonary edema. 3. Angiospasm, or sclerotic arteriolar constriction, may be observed in the retinal arteries of most pregnant women with hypertension.

It is general belief that changes in the retinal arterioles are samples of arterial changes throughout the body. Hallum[8] re-emphasizes this belief in an excellent article based upon personal examination of the eyegrounds of 2,500 pregnant women with hypertension. Unfortunately, space does not permit direct quotation of his descriptions of the spasm of pre-eclampsia and the more permanent sclerosis of chronic hypertensive disease. He also points out that spasm may be superimposed upon arterioles already constricted by the sclerosis of chronic vascular disease. According to him, von Graefe in 1855, four years after the invention of the ophthalmoscope, first described the retinopathy of pregnancy.

The idea that the fundamental pathologic lesion of the pre-eclampsia—eclampsia syndrome occurs in the terminal arterioles is not new. It was first outlined in detail in this country in 1936 by Irving,[10] who explained the production of the pathologic lesions and the clinical signs on the basis of arteriolar spasm. He says that Volhard in 1918 was the first to advance the concept. The year following appearance of Irving's article, Addis[1] in England and Eastman[5] here, made similar observations. Dieckmann[4] mentioned the hypothesis in 1941, but it was not until 1943 that the fundamental nature of arteriolar spasm began to receive attention. Since then, many authors[1, 7-9, 11-14] have affirmed the belief that arteriolar spasm is basic to the development of the pre-eclampsia—eclampsia syndrome. If this can be accepted as a working hypothesis, many of the known facts concerning the disease become explicable on a physiopathologic basis.

The pathogenesis of the kidney and liver lesions, and the development of hypertension, albuminuria, and edema are so well explained by Irving, and more recently by Page,[13] their inclusion here would be repetitious. The remainder of this paper, therefore, will be concerned with attempted explanation of some of the less frequently discussed effects of angiospasm.

Angiospasm

Angiospasm, depending upon location, intensity, and duration, produces varying degrees of tissue ischemia. Mild ischemia of short duration may be tolerated by some tissues without appreciable immediate or permanent damage. On the other hand, malacia, or tissue softening, and necrosis may result from prolonged and severe tissue ischemia. According to Best and Taylor,[2] cells of the cerebral cortex cannot survive complete oxygen lack for more than five minutes, and may sustain definite injury after one-half minute. Cells of the brain stem are less sensitive and may survive total ischemia up to 25 minutes. Obviously, parenchymal cells of kidney and liver are more sensitive than the less highly specialized cells of muscle and integument. The delicateness of highly specialized cerebral cells is attested clinically by the fact that cerebral hemorrhage is found in about 15 to 20 per cent[4] of autopsies on patients dying with eclampsia. Apparently the sequence of events includes: spasm of an end-artery, tissue ischemia, tissue malacia or necrosis distal to the spasm, release of spasm and hemorrhage. Or there may be only sufficient ischemia to produce arteriolar endothelial damage with or without subsequent thrombosis. With these general remarks, consideration will be given to specific locations and entities.

Brain.—Eller[6] described the effect of encephalomalacia in two of the women of the Parkland series. Fig. 1 shows the cerebral tissue damage encountered in a 20-year-old primigravida dying with a terminal fever of 107.6° Fahrenheit on the fourth puerperal day. Fig. 2 shows the extent of the hemorrhage occurring with release of spasm and return of full arterial tension to the softened area. Since the hemorrhage was at the level of the red nucleus in the right midbrain, it explains both the high terminal fever and the fatality.

Fig. 1.—Brain stem tissue of 20-year-old primigravida, B. J., magnification ×110.
Note the well-localized vacuolated area of the neuroglial stroma in the center of the section. The nerve cells have largely disappeared. This is also an area of early necrosis and demyelinization. The injury would seem to be several days old, because early attempts at repair by neuroglial proliferation can be seen. Note the large dark oval bodies in the center bottom of the section. Probably these are degenerating nerve cells.

No one knows the precise mechanism of production of the hypertension or the convulsions of eclampsia. A possible explanation of hypertension might include: generalized cerebral arteriolar spasm, tissue ischemia, cerebral edema, increased intracranial pressure, compression of the medullary center and compensatory hypertension after the mechanism described by Cushing.[3] With regard to the convulsions, perhaps *more than one mechanism* is involved. It is generally agreed that oxygen lack or increased intracranial pressure can produce convulsions. They may also be produced by water intoxication, a fact thoroughly established by animal experimentation and attempts at human therapeutics. It is probable that some of the convulsions occurring in toxemic patients, days after delivery, are due to water intoxication and not at all to the disease.

The Placental Site.—Angiospastic mechanisms similar to those causing intracranial hemorrhage may be invoked to explain hemorrhage in maternal arteries

supplying the sinuses of the placental site. This is a simple reason for accidental, retroplacental hemorrhage and, if true, explains the frequent but not invariable association with acute and chronic toxemic states. On the other hand, it would be foolish to suggest that formation of *all* retroplacental hematomas is due to this cause. Perhaps these mechanisms might also afford explanation for some placental infarcts.

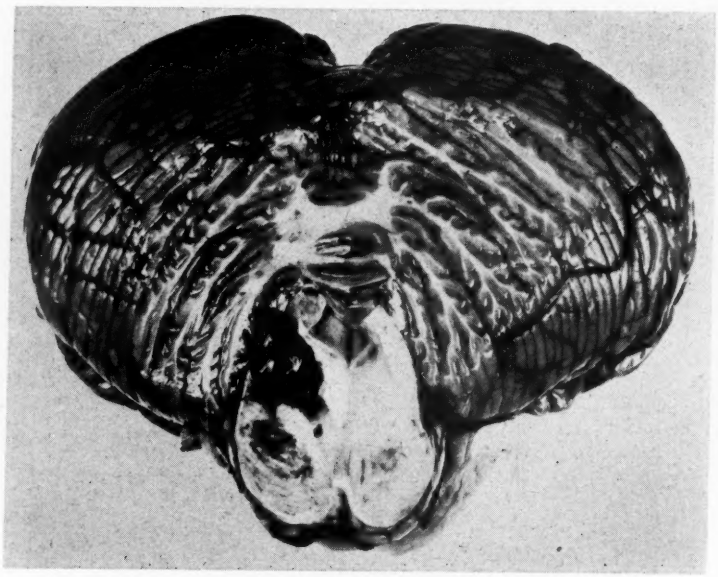

Fig. 2.—Cerebellum and brain stem of patient of Fig. 1. The hemorrhage is in the right midbrain at the level of the red nucleus. Reprinted from Eller.[6]

The not infrequent occurrence of children smaller than compatible with the known duration of pregnancy, or of unexplained stillbirth, is a well-known clinical phenomenon. In the past it has been ascribed vaguely to the "toxicity" of pregnancy toxemia. With acute pre-eclampsia—eclampsia syndromes, long-continued spastic reduction of maternal arteriolar caliber could diminish materially the available supply of nutrient materials. More severe spasm might cause fetal death from anoxia. With chronic, pre-existing hypertensive vascular disease, the known tendency to fetal death toward the end of pregnancy is readily understandable in terms of chronic, sclerotic arteriolar constriction. Superimposition of acute, upon chronic, toxemia would seem to favor appearance of these phenomena centering around the placenta. On the other hand, many toxic women and their infants escape placental difficulties. Perhaps this is so because the chief localization of arteriolar damage or spasm happens to be other than the placental site. Perhaps it is of mild degree, or the enormous compensatory powers of the body tend to nullify damage.

Treatment.—Through the years, treatments for pregnancy toxemia come and go, but always there remain three clinically proved and accepted measures: bed rest, sedation, and interruption of pregnancy. In the light of angiospasm, it is easy to understand the first two. The horizontal position immediately decreases the cardiac load, minimizes antagonism between angiospasm and resulting hypertension, and increases the urinary output. Sedation provides a gentle means of relaxing angiospasm.

Soon after termination of pregnancy, angiospasm ceases. Thus, interruption shortens the duration of ischemia and thereby minimizes the danger of permanent tissue damage.

A final word must be said concerning two treatments: one old, Veratrum viride, and the other new, high spinal anesthesia. Both provide vasodilation, the former generally, and the latter locally below the level of the injected drug. It would seem logical to employ one or both. On the other hand, there is evidence that the hypertension of pregnancy is both attempted compensation and protective response. Partially for this reason, but chiefly because of previous success, we have not yet seen fit to adopt either of these treatments.

Summary

Five toxemic women died on our service during a nine months' period as a result of, or in association with, pulmonary edema. This motivated a change in treatment schedules, and a simple policy of fluid maintenance was adopted. The daily fluid intake, therefore, is now limited to 2,500 c.c. of fluid. Five per cent dextrose in distilled water is the infusion medium when the patient is unable to drink, and no hypertonic solution or plasma is employed. No other treatment feature was changed, and the basic philosophy of ultraconservatism was continued. Since then, no toxemic patient has died and none has developed recognizable pulmonary edema. Twenty-four consecutive pregnant women with convulsive toxemia have recovered and there is a 77.8 per cent fetal survival rate.

Angiospasm was advanced by Volhard in 1918 and by Irving in this country in 1936 as the basic pathologic lesion of eclampsia. Its existence can be seen in the retinal arterioles of most pregnant women with hypertension. It is believed that many of the pathologic lesions and known clinical phenomena of pregnancy toxemia can be explained on this basis.

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Discussion

DR. NEWELL W. PHILPOTT, Montreal, Canada.—I would like to corroborate the statement of Dr. Mengert when he says that large intake of fluid is ill advised in the patient with edema, especially when the kidneys are not excreting to normal capacity. We have had two cases where reactions were of a serious nature. These were severe pre-eclamptic patients with marked edema. After delivery they were given glucose and water with 10 Gm. of

methionine intravenously. There was a withdrawal of fluid from the tissue spaces but there was still a temporary anuria present. This overloaded the circulation with a subsequent right-sided heart failure and creation of a marked pulmonary edema. Fortunately, adequate kidney excretion took place within a few hours and both patients recovered.

With reference to vascular spasm, I shall show one case tomorrow where there was widespread brain damage, presumably caused by persistent vascular spasm and anoxia. This patient was discharged from hospital when she was in a definitely demented condition. The electroencephalogram denoted several large areas of apparent cerebral infarction.

While I still think that water is the best diuretic agent, our experience in Montreal also shows that a rational amount of fluid intake should be administered after taking into consideration the amount of edema present, the condition of the heart, and excretion capabilities of the kidneys.

DR. HOWARD C. TAYLOR, JR., New York City.—Dr. Mengert's view that the toxemias of pregnancy are dependent for many of their manifestations upon angiospasm is no doubt true. There is, however, one aspect of the disorder that has been investigated repeatedly which offers some contradiction. The study of the blood fluid through the kidney during the acute phase of the toxemias of pregnancy has shown no ischemia but an actual increase in the blood flow. I think that toxemia of pregnancy is the only decrease with hypertension in which renal ischemia is not demonstrated by this method.

It is, furthermore, striking that many of these patients who have a hyperemia of the kidney during their acute phase develop an ischemia of the kidney after delivery, providing that the hypertension remained. In other words, the cases subdivide themselves after delivery into those in which there is complete recovery, where the renal blood flow remains normal; and those in which there is a residual hypertension, where the renal blood flow drops to levels characteristic of essential hypertension.

These observations by four independent workers are, I think, of some definite significance, since they indicate that the hypertension of the toxemia of pregnancy is in some way different from that of the nonpregnant individual. There is also a slight indication that at least in one area of the body vasodilatation may be present as well as angiospasm.

DR. RUDOLPH BARTHOLOMEW, Atlanta, Ga.—I would like to call attention to the fact that angiospasm undoubtedly is a very important underlying basis for toxemia of pregnancy but cannot explain all of the phenomena. I would call attention particularly to the fact that in fulminating cases convulsions may occur without much angiospasm. One who notes the condition of the retinal arteries can often find cases of fulminating eclampsia showing a few beginning spasms, and yet these patients are having repeated convulsions.

If the condition of the arteries in the eye is a criterion of that pertaining to the arteries throughout the body, we must admit then that there is some other factor which has not as yet been stressed. I do want to emphasize that the angiospasm is not the entire story.

DR. THADDEUS L. MONTGOMERY, Philadelphia, Pa.—Dr. Mengert's paper supports the thesis that angiospasm, capillary hemorrhage and thrombosis, and local tissue necrosis are important histologic lesions in the underlying pathology of eclampsia. The fact that Dr. Taylor's studies of renal function do not point to a consistent deficiency of circulation in the renal area does not necessarily disprove this now commonly accepted concept. It is well known that vascular changes in one organ may differ very considerably from those in another.

Studies that we have been conducting in our department of cerebral circulation in toxemia of pregnancy help to support the thesis which Dr. Mengert's paper favors. Employing the method of Kety and Schmidt, we have found a general reduction of cerebral circulation, oxygen consumption, and metabolic exchange in the presence of severe pre-eclampsia, eclampsia, and some of the other hypertensive conditions. These findings are to be reported in a short time and will constitute, I believe, the first confirmation of our many theories as to what goes on in the brain in eclampsia.

I would disagree with Dr. Mengert, however, upon the question of the significance of edema in the toxemia patient, not from the point of representing that edema is the cause of the phenomena of eclampsia, but to suggest that important consideration in some of the late and terminal phenomena.

When edema is present and can be reduced the severe pre-eclamptic and eclamptic seem to do much better than the patient who is not edematous. Practically all forms of treatment which we have today have as one of their purposes the reduction of tissue electrolyte, particularly sodium, and the reduction of edema. Even the speaker limits the amount of fluid intake and keeps his patients upon a high-protein and a low-salt diet.

However, in the limited state of our knowledge of this subject one cannot be too dogmatic. The amazing thing about the whole problem of eclampsia and the discussions which arise concerning it is the fact that so many different treatments, apparently diametrically opposed in one direction or another, are so successful in the hands of those who are experienced in the management of this disease.

DR. NEWLIN PAXSON, Philadelphia, Pa.—We have in our work reached the same conclusion, that angiospasm shows a pathologic change in eclampsia. We thought this might account for Stroganoff's theory that the use of an old drug which had been more or less discarded (chloral hydrate) because of fear of damage to the liver, might actually represent an approach both as a sedative and a vasodilator. Therefore, we have been using it in much larger quantities than we have used morphine, feeling that it did not produce any ill effects. And although there might be some danger of liver damage, we believe that the problem is so acute and relatively short-standing, we have used chloral hydrate as our possible answer.

As to the second point, we are following the Smiths' work in regard to a toxin being responsible for the angiospasm. I was wondering if Dr. Mengert would care to correlate any opinions he may have on the investigations of the Smiths in relation to angiospasm?

DR. MENGERT (Closing).—It was my desire to focus attention upon angiospasm and I think that desire was accomplished. There was no claim made that the kidney lesion in itself produced hypertension. I think, of course, that some kidneys do not have a great degree of angiospasm. The intensity of angiospasm varies in different parts of the body. For example, I remember well a patient who had necrosis of, and lost a large part of the right gluteus. At the time we thought it was due to thrombosis. I now believe this must have been due to angiospasm. Why there should have been angiospasm of that particular end artery no one can answer at the present time. Certainly, in the more severely ill patient, as Dr. Taylor suggested, angiospasm is a feature of the syndrome and every one who has written on the pathology of the kidney agrees with this. Fahr, in 1924, spoke of the glomerular ischemia.

Edema is present as extracellular fluid and I think the important thing we must bear in mind in treating these patients is not to bring fluid back into the vascular tree and thereby overload the circulatory system. I do not think that during the immediate convulsive stage it is of importance to worry about the edema. I think the important thing is the effect of the water. I remember a patient I had a hand in treating some years ago where we used all known procedures from hypertonic fluids to blood transfusion and finally this patient went into a stasis eclampticus and died. Now I believe she died from water intoxication. We must remember that water intoxication can produce convulsions and I would like to close on the thought that perhaps some of the convulsions we see in eclamptic patients are the result of the treatment and not of the disease.

THE SECOND STAGE OF LABOR*

III. Number of Pains

L. A. CALKINS, M.D., PH.D., KANSAS CITY, KANSAS

(From the University of Kansas Medical Center)

SOME years ago, we suggested to our house staff that whenever there was doubt as to completeness of dilatation of the cervix, a vaginal examination, under aseptic technique, should be done. This resulted in a lessened frequency of prolonged second stage in our clinic. There was still remaining, however, a higher incidence in the clinic patients than was being observed in our private patients. We, therefore, made it a rule that a vaginal examination should be done when the head did not reach the pelvic floor within thirty minutes after the cervix had been thought to be completely dilated. (We had always operated in the belief that the cervix should not be considered to be completely dilated until it had completely retracted over the head.) It was very apparent, after the initiation of the above rule, that the final stages of cervical retraction were often very slow in the presence of poor labor pains in primiparas. It was also very apparent that a partially retracted cervix could not be palpated, in the anterior half of its circumference, by rectal touch.

Another survey of our records, a little more than a year ago, showed an almost complete absence of prolonged second stage. There was still, however, a marked variation in the duration of this part of the labor. While most of the patients, both primiparas and multiparas, had a quite short second stage, there was still a considerable number of primiparas in whom the second stage exceeded one hour. A survey of the latter group, separated from the larger fraction of the patients, showed a remarkably high incidence of long interval between pains (four to as much as eight minutes). We immediately wondered whether the prolonged second stage could not be partially explained on the basis of this long interval. We had previously found[1] that intensity of uterine contractions was a highly important item in the duration of the second stage. It is quite apparent to everyone that pains of good intensity are usually close together. It is also evident that pains at infrequent intervals are usually of poor intensity. Since there is no simple method of measuring intensity of uterine contractions accurately,† it was difficult to tell whether intensity or frequency was the more important consideration. The very fact that the results were measured in minutes introduced a third variable—time. It occurred to us, therefore, that we should, perhaps, try to eliminate both the frequency factor and the time factor from our consideration. This could very readily be done, if we noted the intensity of the pains, and then counted the number of pains, and used as our measure of the duration of the second stage the number of pains,

*Read at the seventy-first annual meeting of the American Gynecological Society, Williamsburg, Virginia, May 24 to 26, 1948.

†We have called contractions during which the uterus cannot readily be indented at the height of a contraction as "good", in comparison with contractions during which the uterus is readily indented, which we have called "poor."

instead of the number of minutes. This is very logical, since fifteen pains at four-minute intervals, thereby consuming one hour, should not logically be expected to accomplish more than fifteen pains at two-minute intervals, which would consume only half as much time. It should be noted here—somewhat parenthetically—that fifteen pains at one-minute intervals do not actually accomplish as much as fifteen pains at two-minute intervals. This is probably due to an insufficiently long period of relaxation, and might be considered as subclinical tetany.

In the last year and a half, since the above plan was adopted, the vast majority of our records contain the number of pains, in addition to the previous data theretofore included. Not always has the vaginal examination been made, although there has developed somewhat of a tendency to examine most patients by vagina if the head does not reach the perineum immediately after the cervix is thought to be dilated. We have not discouraged this tendency, because, in a teaching clinic, we feel it highly important to impress upon everyone that such is the normal course of events.

TABLE I. STATION AT COMPLETION OF DILATATION

NO. OF PATIENTS		ON PELVIC FLOOR		ABOVE	
		NO.	PER CENT	NO.	PER CENT
Primiparas	790	558	71	232	29
Multiparas	1178	909	77	269	23

Among 790 primiparas with occiput presentations (Table I) the head was found to be on the pelvic floor at the time the cervix was completely dilated in 558 patients (71 per cent). In 59 others, the head reached the pelvic floor either before or during the course of the next uterine contraction. In other words, the head was on the perineum at the time the cervix was dilated, or with the next pain, in a total of 617 out of 790 primiparas (78 per cent). Similar figures for multiparas showed 909 of a total of 1178 on the perineum at the time the cervix was dilated (77 per cent). One hundred sixty-four others reached the perineum on or before the completion of the next contraction. A total, then, of 1073 of the 1178 multiparas had the head on the perineum at the completion of dilation, or within one pain thereafter, (91 per cent). One cannot help but wonder whether the strictly normal course of events does not call for the head being on the perineum at the time the cervix is completely dilated. One cannot, however, reason conversely that the head on the perineum means complete dilatation, as we see a definite percentage of our patients with the head on the perineum for a considerable time before the cervix is completely retracted. Two to three per cent of all patients show this. In one group (primiparas with poor first-stage pains), 8 per cent will have the head well down on the perineum by the time there is 7 to 9 cm. dilatation.

We have previously urged[2] that the second stage be considered as being composed of two phases: one, a descent phase, and two, a pelvic floor phase. From the above, it is quite apparent that at least 70 odd per cent of both primiparas and multiparas have the head on the perineum at the time the cervix is completely dilated. These patients have only a pelvic floor phase in the second stage. The remaining 20 odd per cent, of both primiparas and multiparas in this present series, did not bring the head to the pelvic floor for a variable time after the cervix was completely retracted. As will be shown, the number of

pains required to complete this descent phase varied from none to ten. Following completion of descent, these patients then had the same pelvic floor phase characteristic of the larger group. The total duration of the second stage for this smaller group, who had both a descent phase and a pelvic floor phase, cannot logically be compared directly with the total duration of the larger group, which had only a pelvic floor phase.

TABLE II. PRIMIPARAS, DESCENT PHASE

NUMBER OF PAINS	0-1	2-4	5-10	OVER 10
Good pains	32 per cent	37 per cent	31 per cent	
Poor pains	23 per cent	42 per cent	33 per cent	2 per cent

Study of the descent phase in the 232 primiparas (Table II), showed that the descent was a bit more rapid with good pains than with poor ones but that, even with poor pains, all had reached the pelvic floor in ten pains or less. Two per cent—a total of three patients only—according to the records, showed 13, 15, and 20 descent-phase pains, respectively. In none of these three patients were the pains actually counted, but only "estimated," and in none of the three was a vaginal examination done. Critical review of these three records would seem to indicate that only the last one of the three probably had more than ten pains to reach the pelvic floor. In the 269 multiparas (Table III), the vast majority had reached the pelvic floor within six pains, and all save two patients had reached the pelvic floor within ten pains or less. One of these two patients was "estimated" to have had fourteen contractions in her descent phase, and the other one sixteen. No vaginal examination was made in the first, and the record is uncertain as to whether a vaginal was made in the second. Assuming that the second patient did actually have more than ten pains in her descent phase, we then have one primipara out of 790 and one multipara out of 1178 who required more than ten pains to reach the pelvic floor after complete dilation of the cervix.

TABLE III. MULTIPARAS, DESCENT PHASE

NUMBER OF PAINS	0-1	2-4	5-10	OVER 10
Good pains	67 per cent	29 per cent	4 per cent	
Poor pains	57 per cent		13 per cent	1 per cent

As stated above, the pelvic floor phase of those patients having a descent phase was in no way different from the larger group, who had no descent phase. The 1174 multiparas (Table IV) were found to have completed the pelvic floor phase in the vast majority of cases in about three pains, and in virtually all instances in ten pains. Again, good pains accomplished the end result more quickly than poor pains, but the difference between good pains and poor pains was not nearly so marked as we had previously thought, further emphasizing the value of pain measurement over minute measurement. Eight patients only (less than 1 per cent of the total), according to the records, required more than ten pains. (One patient, previously delivered by cesarean section and, therefore, a primipara for purposes of this discussion, was also inadvertently included in Table IV.) Six of these eight patients were said to have had 12, 13, 13, 14, 14, and 15 pains, respectively. The duration in minutes of the second stage in these same patients was 20, 20, 24, 28, 28 and 30 minutes. In most instances, the pains were not actually counted, but the number only estimated.*

*While the house staff has been very diligent in counting the pains, it is only natural that they should forget occasionally. As a matter of fact, intern and resident usually keep separate count, and when they disagree, an estimate is the result.

In at least three of the six patients, no vaginal examination was done. In three cases, the pains were said to be one to one and one-half minutes apart, which, as noted above, is not a desirable situation. It seems doubtful whether any of these six patients had materially more than ten pains in her pelvic floor phase. The remaining two patients certainly had more than ten pains.

TABLE IV. MULTIPARAS, PELVIC FLOOR PHASE

NUMBER OF PAINS		0-3		4-6		7-10		OVER 10	
		NO.	PER CENT	NO.	PER CENT	NO.	PER CENT	NO.	PER CENT
Good pains	602	470	78	100	17	31	5	1	0
Poor pains	572	386	67	135	24	43	8	8	1

One, a twenty-five-year-old gravida ii, para i, had the head on the perineum three minutes after completion of dilation (one pain), and delivered spontaneously thirty-six minutes later, after eighteen pains. She was normal in all respects; the baby weighed 3,640 Gm.; and the head was completely rotated at the time the head reached the pelvic floor. She was said to have had "very poor" pains. She had been given 2.5 mg. of Pontocaine in 0.5 c.c. of 10 per cent glucose intraspinally. We do not feel that this minimal dose saddle block materially reduces the effectiveness of second stage pains, but, like any other anesthetic, it does have some effect. The other patient, a thirty-year-old gravida ii, para i, required thirty-five minutes (ten pains) to reach the pelvic floor, at which time the head rotated posteriorly and was delivered after twenty-nine very poor contractions with the aid of low forceps. (It should, perhaps, be stated here that forceps were used only five times in the delivery of the 1174 multiparas). According to this patient's history, this pregnancy terminated at the end of thirty-three weeks, and the attendant was quite surprised to find the baby weighed 3,100 Gm. This was quite readily explained, however, when it was noted that the placenta weighed 780 Gm. The infant did, throughout the neonatal period and for a considerable time thereafter, react like a premature infant—required incubator care, etc. While it is, therefore, possible for a multipara to require more than ten pains to deliver the baby over the perineum, it is of rare occurrence in this present series.

TABLE V. PRIMIPARAS, PELVIC FLOOR PHASE

NUMBER OF PAINS		0-10		11-20		21-30		OVER 30	
		NO.	PER CENT	NO.	PER CENT	NO.	PER CENT	NO.	PER CENT
Good pains	302	242	80	60	20				
Poor pains	488	269	55	175	36	39	8	5	1

The survey of the pelvic floor phase in primiparas also produced very interesting data. Three hundred two of these primiparas (Table V) were said to have good second stage pains. Two hundred forty-two (80 per cent) of these were delivered within ten pains or less. The remaining 60 (20 per cent) were delivered in most instances in fifteen pains or less, and in all cases within twenty pains or less. Only five of the 302 patients had forceps deliveries, thus reflecting our previously gained confidence that primiparas with good pains will promptly deliver themselves spontaneously. Two of these five forceps cases might have had a few more than twenty pains had the forceps not been used. One can, however, say very confidently that all primiparas, with good pains, will deliver themselves over the perineum in twenty pains or less.

Four hundred eighty-eight primiparas were said to have poor second-stage pains. A little more than half of these patients were delivered in ten pains or less. Another thirty-six per cent were delivered in the second ten-pain period. Eight per cent required twenty-one to thirty pains, and 1 per cent—5 patients—

required more than thirty pains. Three of these five patients were eventually delivered with forceps, and all of them required more than an hour, except one, who was delivered at the end of forty-six minutes. The incidence of forceps in this poor-pain group is as follows: of the 269 patients delivered in the first ten pains, 39 were delivered with forceps; and 17 of the 175 in the eleven to twenty pain group were similarly managed. This relatively higher rate of forceps exhibition is the result of our previously gained impression that primiparas, with very poor pains, are quite unlikely to deliver themselves spontaneously in a reasonable period of time. This present study has gone a long way toward establishing the contradiction of that idea, since 444 (less a few of the forceps cases) are shown to have delivered themselves within 20 pains or less. Of the remaining 44 patients, 39 were delivered between 21 and 30 pains, six of these by forceps. Five had more than 30 pains, and three of the five were delivered by forceps. It seems, on the basis of this study, that it is rather futile to expect a patient to deliver herself spontaneously if she has not done so within thirty pains. It should be noted, however, that the five patients having more than thirty pains in this present series constitute only 1 per cent of those having poor pains, and slightly more than one-half of one per cent of the total number of primiparas. Similarly, it might be noted that the 44 patients having more than twenty pains constitute about 5 per cent of the total number of primiparas.

Discussion

In other words, the primipara, with pains at two-minute intervals, will nearly always have delivered herself within forty minutes. The primipara, with pains at three-minute intervals, can be expected to deliver herself within one hour. The primipara, with pains at four-minute intervals, will naturally require up to eighty minutes, even if the individual pains are of good intensity.

Conclusions

1. Complete retraction of the cervix as a measure of the end of the first stage, or of the beginning of the second, leads to a better understanding of the physiology of the second stage and a better clinical judgment of its progress.

2. Measurement of the duration of the second stage by number of pains, rather than by number of minutes, is more logical and, in our hands, a much more satisfactory method of measurement.

3. Most primiparas can be expected to deliver themselves spontaneously, after the head reaches the perineum, in twenty pains or less.

4. A simple second-stage formula might be stated as follows:

All patients, primiparas and multiparas, will complete their descent phase in ten pains or less.

All multiparas will complete their pelvic floor phase in ten pains or less.

Primiparas, with good pains, will complete their pelvic floor phase in twenty pains or less. Primiparas, with poor pains, will complete their pelvic floor phase, in nearly all cases, in thirty pains or less.

References

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Discussion

DR. ROBERT A. ROSS, Durham, N. C.—In a recent study at Duke University a listing was made of the number of pains rather than judging labor in terms of hours or minutes. The results are in accord with Dr. Calkins' observations. We have long held the thesis that, perhaps, the best way to teach obstetrics is to have the student sit by the laboring woman's bedside with his hand on her abdomen. In this way, he can judge not only the duration and interval of the pains, but also their intensity. From the observations of Rucker, Murphy, and Torpin, we know that pains may not be productive. They also showed that the rest period between pains was just as important as the pain itself. The essayist has re-emphasized this point. We must also recall the behavior of the uterus in prematurely induced labor as compared to normal labor.

Another point is the inability to judge the dilatation and, more important, effacement of the cervix by rectal examination alone. Surely, in our efforts to teach asepsis, we do not examine our patients by the vagina often enough to evaluate properly the behavior of the cervix. Too often when the patient is on the delivery table and asleep, only a thin or not completely dilated cervix is present. The essayist properly calls for an examination by vagina whenever the patient has not brought the baby to the vulva after a period of hard pains. He also distinguishes between a patient who has the fetal head well in the pelvis, without pain, when the labor may be inordinately long and perplexing, and the patient who starts labor with the head unengaged and carrying on in fine fashion.

The incidence of forceps delivery is noteworthy and no doubt springs from listing the number of pains rather than time of labor. Several years ago we had our resident in a general hospital, list the time of day, or night, of all forceps deliveries. The result was as expected. The tired, harassed doctor delivered more patients by forceps before mealtime, bedtime, nad office-hour time than at any other. The essayist's observations should help in anticipating the time of birth.

DR. PHILIP F. WILLIAMS, Philadelphia, Pa.—Dr. Calkins' studies of the progress of labor which he has presented in recent years have been of much interest. In the present essay he has offered us a very simple rule by which one can measure numerically by contractions the degree of effort needed to bring about descent and expulsion of the fetus. It might seem worth while to substitute the formula which he has derived from a fairly large sampling of patients for the time-honored formula of two hours in what we have regarded as the second stage, or thirty minutes with the head on the perineum and no progress, to indicate the necessity for artificial delivery.

I am uncertain, however, as to whether this group of nearly 2,000 women represents a selected group of consecutive cases. No mention has been made of borderline cases. Again, the age of the patient or physical condition, the size of the baby, and the fetal position do not seem to have occasioned any delay. All these factors would seem to occasion more marked variation from the conclusions as to the muscular effort required for descent and expulsion. The incidence of forceps deliveries in the group reported is indeed quite low.

Dr. Calkins' indication for making a vaginal examination is excellent. Certainly, rectal examinations are inconclusive in many instances in determining if the cervix has retracted over the head. The ease of rectal examinations and the avoidance of preparation of both patient and physician and a possible slight increase in morbidity in vaginal examinations possibly make us a little lazy in determining the exact state of the cervix. Very often when the cervix is felt by rectal examination to be fully dilated and then vaginal examination is made we find a very thin cervix, 6 or 8 cm. dilated and probably having very little muscular fiber in it. In reality, the muscular cervix has retracted over the head and the thin mucous membrane layer is still present and retracts on almost the slightest stretching or pushing. The obstructing anterior cervical lip, when pushed over the head and held there during one pain, is often followed by almost immediate delivery.

A large series of healthy, native-born American women in good nutrition and condition, with no pathologic processes, would probably deliver themselves spontaneously in a manner equal to the series Dr. Calkins has reported. But I think we would find in an extensive practice of mixed nationalities, fearful of labor, elderly so far as the first pregnancy is concerned, and demanding and receiving many of the widely prevalent methods of sedation or anesthesia, that their necessary effort to complete the second stage would come far beyond the number of pains in Dr. Calkins' series. I would be interested to know if Dr. Calkins regards the women who had more than thirty pains in the pelvic-floor phase to have had secondary inertia, and if any of his patients could be considered as having had primary inertia.

If we must examine a woman vaginally to determine complete retraction of the cervix as a determination of the physiologic end of the first stage, which is an excellent suggestion, we will probably have a large increase in the number of vaginal examinations to determine the progress of labor, but if we adopt the formula suggested we may not have as many forceps deliveries as are practiced in many clinics.

DR. RUDOLPH W. HOLMES, Charlottesville, Va.:—In 1893, Kroenig and Ries independently wrote articles which extolled the merits of rectal examinations in labor. The history of rectal examinations is an interesting one. Textbooks and journal pages gave scant publicity to their advantages, so that from 1893 to 1915 there was not one formal paper on the subject. Yet, the procedure became a near routine throughout the world without the aid of publicity; its growth was insidious. I wrote a paper in 1915 on the advantages of rectal examinations, based entirely upon my experience as a routine in my own work, and as a method required by my subordinates in various hospitals. To the latter, a vaginal examination was barred except on a special permission.

I do not believe I am prejudiced in its favor—I merely express an opinion based upon my own experience. I still believe that rectal examinations will elicit all needful information in the vast majority of cases; when a failure does occur, usually it will be found that the findings from a vaginal touch will be equally futile; when this does happen, manual examination through the vagina may be imperative. I believe that most antagonists to the method have not given the method a full trial. Abdominal palpation and rectal touch are without danger; vaginal examinations do carry a menace from infection. I express myself strongly as the essayist reflects an unfortunate retrogressive trend as regards methods of investigation.

DR. CALKINS (Closing).—Of course, this was not a paper on the first stage of labor and therefore did not deal with the retraction of the cervix. It was not a paper on anesthetics but these patients did have some form of analgesia as well. Too much anesthesia will prolong labor, it should be stated—both first and second stages—and where we have used too much anesthesia a longer labor has been the result.

This was not an attempt to substitute vaginal for rectal examinations. I quite agree that up to the final stages of dilatation the patient may be very properly and appropriately handled by means of rectal examinations, but my point was that in many instances the cervix is thought to be properly dilated when it is not and I believe a vaginal examination is less dangerous than forceps delivery.

FETAL MORTALITY IN BREECH DELIVERIES*

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IT IS commonly thought that breech presentation, while having little effect upon maternal mortality, and small effect upon maternal morbidity, definitely increases the danger to the fetus, and that this added risk over vertex presentation is due largely to asphyxia and birth injury. The fact that the birth of the child must occur within a few minutes after expulsion to the level of the umbilicus, or compression of the cord may occur, also often results in birth injury from efforts on the part of the obstetrician to overcome dangerous delay in delivery.

There are also other hazards to the fetus, information about which has not been so widely disseminated. In order to gather more data as a background for better management, we have reviewed the recent literature and studied a moderately large group of breech cases occurring in 25,532 deliveries, during two five-year periods, 1933 to 1937, and 1942 to 1946.

The commonly reported incidence of breech presentation is from 2.1 per cent[23] to 6.32 per cent.[36] In our group of 25,532 deliveries, breech presentations occurred in 1240, or 4.8 per cent. At variance with the usual statements relative to etiological factors, pelvic contraction, as an obstacle to engagement of the vertex, seemingly has little or no effect in the production of breech presentation. Pelvic contraction occurred in only 2.7 per cent, actually a rather low incidence. In our experience, other commonly stated causes, such as placenta previa and the toxemias, are important only as a cause of premature labor. We were able to find no statistically discernible cause for breech presentation other than prematurity and twin pregnancy.

Vartan[57] asserts that the reason why breeches persist until term is not to be sought in factors which prevent the head from engaging but are those which prevent spontaneous version from taking place and believes that extension of the legs is a prime factor, by giving the fetus an extended attitude.

Fetal Mortality

It is generally conceded that breech presentation entails more danger to the fetus than does vertex, but there has been considerable disagreement as to the exact degree of this added risk. There is also some debate as to the parts played in this increased mortality by the presentation itself and by other factors which might be the cause of the presentation. In an attempt to arrive at an answer to the question, different calculations have been used which make comparisons difficult and have led, at times, we believe, to doubtful conclusions. A common error has been the acceptance of the gross or total fetal mortality as representing the percentage risk for all groups of breech presentations.

*Read, by invitation, at the seventy-first annual meeting of the American Gynecological Society, Williamsburg, Virginia, May 24 to 26, 1948.

Gross Fetal Mortality.—In consulting the literature, six authors gave as gross fetal mortality all stillbirths and neonatal deaths occurring from the twenty-eighth week of pregnancy to term. These mortalities varied from 11.5 per cent[1] to 35.3 per cent.[29]

In our cases for the five-year period 1933-1937, among 773 breech deliveries, there were 244 stillbirths and neonatal deaths, 31.6 per cent. The vast majority occurred among very immature babies, although a considerable number were dead on admission or had malformations incompatible with life. For the five-year period 1942 to 1946, there were 51 deaths among 467 deliveries of breech cases, 17.4 per cent.

Corrected Fetal Mortality.—Since it is obvious that a considerable number of deaths occurring in the gross rate cannot be attributed to the presentation, deductions have been made in order to determine the fetal mortality due to the presentation itself. It, therefore, seems reasonable to deduct (1) nonviable prematures (less than 1,500 Gm., 3 pounds, 5 ounces), (2) babies with fatal malformations, and (3) those who were already dead on admission. Correction by deduction for deaths due to prolapsed cord and to maternal complications, however, seems indefensible. Whether or not twin pregnancy, with one or both fetuses presenting by breech. should be deducted or included has been debated in the literature. Actually, this is of little importance since the small number of multiple pregnancies would have little statistical effect. We have included only cases in which the first twin presented by breech and considered it as one case.

With the above corrections, eight reports reviewed showed mortality rates of 5.38 per cent[33] to 22.7 per cent.[7] Our mortality for the 1933 to 1937 period showed 53 deaths in 538 cases, or 9.9 per cent, and for the 1942 to 1946 period was 30 deaths among 446, or 6.7 per cent.

Corrected Premature Mortality.—It is a fairly common belief that breech presentation is especially dangerous for the premature child. This danger has been ascribed to the chance of delay in delivery of a relatively large head through a birth canal inadequately prepared by the small body and shoulders. This has probably been too much emphasized by the inclusion in many reports of very immature fetuses who would have little chance to survive with any presentation. If we arbitrarily assume, as is customary, that birth weights between 1,500 Gm. (3 pounds, 5 ounces) and 2,500 Gm. (5 pounds, 8 ounces), for babies alive on admission and having no gross developmental defects, represents viable prematurity, we were able to find in the literature mortality rates varying from 14.3 per cent to 48.6 per cent.[32, 33, 36] Morton[32] also states that the general mortality for all premature babies in his hospital was 36.8 per cent. In our group of such babies there were 145 with 37 deaths, 24.1 per cent. Forty-five weighed less than 4 pounds, with 42.6 per cent mortality; 58 weighed between 4 and 5 pounds, of whom 19.3 per cent died, and 42 weighed over 5 pounds but less than 5 pounds, 8 ounces, with 10 per cent deaths. If it is remembered that our figures include both stillbirths and neonatal deaths, there is apparently no indication of a definitely increased risk for viable prematures presenting by breech. In this connection, with very premature babies (3 pounds, 5 ounces, to 4 pounds) it is interesting to note that the mortality rate for the first five-year period (1933 to 1937) was 55 per cent and for the last five-year period (1942 to 1946) was 37.5 per cent, due, we believe, to better premature care in the later group.

Corrected Term Mortality.—Variations of opinion as to what constitutes a full-term fetus have given rise to considerable confusion in the literature as to the interpretation of results, and, at times, to false conclusions. Some authors apparently relied on the questionable estimate of maturity from the reported

last menstrual period. Others made no mention of, or were too indefinite concerning, size and maturity. The majority of authors, however, agreed that a fetus weighing 2,500 Gm. (5 pounds, 8 ounces) or over is mature insofar as its ability to survive is concerned. We have reviewed ten reports in which the results for term babies were computed by this criterion (with deduction for gross malformations and fetuses dead on entrance). There was considerable variation in results, especially where small numbers of cases were concerned. Mortality rates for 200 cases or more varied from 8.5 per cent[4] to 12.5 per cent.[17] Our stillbirth and neonatal mortality in both groups of cases (1933 to 1937, 1942 to 1946) was 42 deaths in 800 deliveries, or 5.2 per cent.

TABLE I. COMPARATIVE FETAL MORTALITY (FOR VIABLE TERM BABIES)

	GENERAL FETAL MORTALITY (PER CENT)	BREECH MORTALITY (PER CENT)
1933 to 1937	1.8	6.5
1942 to 1946	1.1	3.5
Both periods		5.2

Special Factors in Breech Mortality

Prolapse of the Umbilical Cord.—Authors reporting the incidence of prolapsed cord vary in percentages from 0.9[42] and 11.9.[35] Among a total of 5822 cases of breech in the literature reviewed, this complication occurred in 2.9 per cent. Among our 984 cases with viable babies, the cord prolapsed 31 times, or in 3.2 per cent. Caldwell and Studdiford[3] gave an incidence of 0.5 per cent in 6947 cases for all positions, and this is close to the accepted average. It is apparent, therefore, that prolapsed cord in breeches is about six times that for all presentations.

The importance of prolapsed cord in relation to fetal death in breech presentations, then, is evident. In 159 cases reported by seven authors, there were 68 fetal deaths, about 43 per cent. So definite is the fetal danger that Studdiford[39] and Sherman[38] strongly advise routine vaginal examination on rupture of the membranes in order to be immediately aware of the complication. In our 31 cases there were 10 deaths, or 12 per cent. In other words, approximately 3 per cent of the cases with prolapsed cord are responsible for 12 per cent of the total mortality.

Contracted Pelvis.—The danger to the fetus, with contracted pelvis, is recognized throughout the literature. Particularly dangerous are the mild contractions which are frequently overlooked, with disastrous results. As yet, there seems to be no adequate method which provides a comparison of the size of the fetal head in the fundus with that of the pelvis. The existence of cephalopelvic disproportion, then, is often not discovered until late in the second stage of labor, when the child is seriously endangered from asphyxia or from urgently indicated attempts at delivery. The seriousness of the complication as a factor in breech presentation is evident from various reports.[3, 5, 12, 17] As an example, Gordon, Garlick, and Oginz[17] found a 31.7 per cent fetal death rate in primiparas and 32.6 in multiparas. In the material here reported, we found 22 contracted pelves (2.7 per cent of term cases), of which 70 per cent were delivered by cesarean section. There were no fetal or maternal deaths.

Birth Weight.—The weight of breech babies we believe to be an important factor in mortality rates. Most writers are in agreement that large babies presenting by breech have a high death rate. Mohler[29, 30] reports that 50 per cent of primiparous breech babies weighing 8 pounds or over, died. Experience of others also shows that there is a higher-than-average death rate from small, but viable babies. The best results are obtained with babies of medium weight.[7, 16, 52] Our result in the first group of cases would tend to confirm this:

TABLE II. MORTALITY RATES AND BIRTH WEIGHTS

	5 LBS. 8 OZ. TO 5 LBS. 15 OZ. PER CENT DIED	6 LBS. TO 6 LBS. 15 OZ. PER CENT DIED	7 LBS. TO 7 LBS. 15 OZ. PER CENT DIED	8 LBS. TO 8 LBS. 15 OZ. PER CENT DIED	9 LBS. AND OVER PER CENT DIED
Primiparas	14.8	7	1.4	16.7	50*
Multiparas	6.1	1.4	3.4	7.9	17.9
All cases	10.0	4.4	2.5	11.3	20.0

*Only 2 cases.

Frank Breech.—In previous studies, Siddall and I[52, 53] drew attention to the fact that several authors have expressed the belief that there is a higher fetal mortality associated with frank breech deliveries. In our first group of cases, 1933 to 1937, we were unable to confirm this and even stated that, in our experience, after grouping as to parity and further subdivision as to premature and term babies, there was without exception a *lower* mortality for frank breech.

In our 1942 to 1946 cases with viable babies, I am unable to confirm a lower death rate for frank breech except for premature primiparas and term multiparas. For premature primiparas. the fetal death rate was 12.5 per cent for frank breech and for other breech presentations, 14.2 per cent. For term multiparas, the percentage was 0.0 for frank breech and for other breech presentations, 3.5 per cent. It would seem, therefore, that frank breech is associated with little if any added risk to the fetus.

Parity.—Statements in the literature vary considerably in regard to parity as a factor in fetal mortality, although it might naturally be expected that they would ascribe a higher rate for primiparas. And this seems to be borne out by the available data. Nevertheless, King and Gladden[22] report mortality rates of 7.7 per cent for primiparas and 12.5 per cent for multiparas, for babies weighing over 5 pounds. They offer in explanation the fact that dead babies in this group averaged 1 pound, 4 ounces heavier when born of multiparas.

Our experience is shown in Table III.

TABLE III. STILLBIRTH AND NEONATAL MORTALITY RATES FOR VIABLE BABIES OF PRIMIPARAS AND MULTIPARAS, 1933 TO 1937 AND 1942 TO 1946

TOTAL MORTALITY		PREMATURE MORTALITY		TERM MORTALITY	
PRIMIPARAS (PER CENT)	MULTIPARAS (PER CENT)	PRIMIPARAS (PER CENT)	MULTIPARAS (PER CENT)	PRIMIPARAS (PER CENT)	MULTIPARAS (PER CENT)
5.7	7.8	13.8	31.9	4.7	3.4
		1942 to 1946			
3.1	5.0	13.3	31.0	1.5	1.4

An interesting and surprising finding is the high mortality of premature babies of multiparas. This has been noted elsewhere in the literature.[1] It seems obvious that this is responsible for a reversal of the relative results for the combined and for full-term deaths. A partial explanation can be found in the greater proportion of large prematures (5 pounds to 5 pounds, 7 ounces) delivered by primiparas, 40 per cent as compared to 23 per cent by multiparas. It is also possible, as term babies are larger in multiparas, that premature babies of the same weight might actually be less mature and therefore more likely to die.

Length of Labor.—There is little evidence in the recent literature[2, 12, 24, 27, 37] to support the belief that breech labor is likely to be prolonged with adverse effect upon the fetus. In our groups, the average length of labor for women whose babies weighed 5 pounds, 8 ounces and over and died, was 20 hours, 15

minutes. There were two cases of much-prolonged labor due, apparently, to primary inertia that contributed to this average. Without these two cases, the average length of labor was 12 hours, 20 minutes. From the data available, it is questionable that breech presentation, in itself, is associated with sufficient prolongation of labor to be a factor in fetal mortality.

Age of Primiparas.—We have always felt apologetic when using the term "elderly primipara," especially when applied to women in their thirties, as an indication for various obstetrical procedures. Nevertheless, the literature[2, 4, 17, 42] and our own experience show an increasing death rate for breech babies of these women; and this is especially true if the babies are large. From 1933 to 1937, for term babies of primiparas over 30 years, the mortality was 13.3 per cent compared to 6.8 per cent for the younger group. In our 1942 to 1946 group, the death rate was 10.5 per cent for primiparas of 35 years or more, as compared to 5.8 per cent for those under 30.

Early Rupture of the Membranes.—We have been unable in the material at hand to show any increased fetal risk for dry labors with breech presentation. There seemed to be the same accelerating effect on labor, insofar as we could judge, due to early rupture of the membranes, that has so frequently been observed for vertex presentations. In our opinion, the increased risk is due to the danger of prolapse of the cord with early rupture of the amniotic sac, rather than to any effect upon labor.

Skill of Attendant.—It has been said that there is "no substitute for experience" and this dictum holds true, we believe, in the management of breech cases. In previously quoted figures in this report, we have shown increasingly better net fetal death rates in later years. In the first series, 1933 to 1937, approximately two-thirds were delivered by internes and residents in training, with the usual supervision. In the 1942 to 1946 group, at least 95 per cent were delivered as private patients by a staff composed largely of diplomates of the American Board of Obstetrics and Gynecology.

Other factors affecting the net mortality rate were the same for both groups. Pertinent to this is Dieckmann's statement[62] that his corrected mortality rate for term babies is 4.2 per cent and Tomkins' report[56] of 2.7 per cent net mortality in a group of patients, all of whom were delivered by Board members. The fact remains, however, that breech delivery, in any hands, is associated with a higher-than-average fetal mortality.

Treatment

It is not necessary, we believe, in a study of this kind to give detailed management of breech presentation during labor and delivery. While we do not intend to ignore the value of proper management, this can be found in all textbooks and in numerous papers. There are, at times, interesting new approaches being advocated and several of the older procedures might well be re-examined. Among these are:

Prophylactic External Version.—As we have shown that breech presentation, even with expert management, is associated with an inevitably increased fetal risk, it becomes obligatory at least to consider prophylactic external version for conversion to a more favorable position. This procedure has been objected to on grounds of the risk involved, which might arise from separation of the placenta and from entanglement of the umbilical cord; and on the grounds that there is a certain percentage of failure or reconversion back to the original breech presentation. The degree of risk involved, of course, far outweighs all

other objections. This apparently is slight, when done gently and without anesthesia, as shown by preponderance of evidence in the literature, seventeen out of twenty-one authors recommending it.

External version, however, is not universally successful, especially if done early. Vartan[50] states that breech presentation is common until the 34th week, so common that it must be regarded as a normal occurrence at certain stages of pregnancy, and found 680 spontaneous conversions to vertex among 1000 cases after the thirtieth week. The majority of these had occurred by the thirty-fourth week, although 28 were spontaneously converted to vertex in the thirty-fifth and thirty-sixth weeks. Spontaneous version is rarely followed by reconversion to the original breech (only 5 per cent) while Ryder[55] finds that reconversion occurs in 33 per cent of external versions. There is a tendency for a higher percentage to reconvert if they are done early, while, after the thirty-first to thirty-second week, this tendency diminishes. External version then, while technically easy, is not universally successful, but we believe deserves an adequate trial in an effort to lower fetal mortality from breech presentations.

Cesarean Section.—It is well to recognize at the beginning of any discussion of cesarean section for breech cases, that it has, with few exceptions, a fetal indication only. We have stated before, and are borne out by the literature, that there is very little, if any, added maternal risk from breech delivery. There is, however, a definite added risk to the mother from cesarean of from three to ten times that of vaginal delivery. It also carries with it possibilities of trouble in future pregnancies. The subject then resolves itself around the question as to what degree of fetal danger permits an added maternal risk, by abdominal section, for its relief. We have shown, I think, that, in at least three groups of cases, there is so great fetal loss that cesarean should be considered if prophylactic version fails.

Contracted pelvis, even in the very mild degrees, is especially dangerous to the child presenting by breech. As mentioned before, we have found no reliable method of estimating disproportion with the head in the fundus. Therefore, we think that delivery by cesarean section is indicated from the fetal standpoint whenever any degree of disproportion seems probable. In our twenty-two full-term cases, section was done in fifteen and no babies or mothers died. We realize that it is impossible to draw conclusions from so small a group of cases, but our results are apparently different than those found in reports where a high percentage of sections was not done.

As noted before, fetal mortality is high in primiparas over 30 years of age, and particularly so after 35 years. In the primiparas over 35, there is frequently such a great desire for a living child as at least to merit consideration of delivery by section. We believe that the prospective parents, after explanation of the relative fetal risks, should have a voice in the choice of procedure.

From data previously presented, birth weight appears to be an important and frequently overlooked factor in fetal mortality. Babies of medium weight show only a moderately increased mortality, but for larger babies (8 pounds and more) the rate becomes excessive, particularly for primiparas. We realize that there is no accurate method of estimating the size of the unborn child, but we can usually classify the fetus as large, medium, or small. Should the size be large, in the interest of the child and from all evidence collected, we believe that careful consideration should be given to delivery by cesarean section, particularly if the patient is a primipara.

It is evident that combinations of two or more of these factors make section more likely to be the procedure of choice.

Early Breech Extraction.—As early as 1926, Irving and Goethals[21] reported a reduction of fetal mortality in breech presentation by the use of routine breech extraction as soon as the cervix was completely dilated and Goethals[15, 16, 45, 46, 48]

has continued the discussion in subsequent publications. He states that extraction is undertaken after, but not necessarily immediately after, attainment of full dilatation with respect to the breech, and indicates that stillbirths and neonatal deaths have been reduced 50 per cent by this policy, his personal rate being 2.3 per cent. Potter, Erving, and Brown[60] believe that no patient with breech presentation, after complete dilatation of the external os, should be allowed to proceed into the second stage of labor. On the other hand, Caldwell and Studdiford,[3] after a trial, opposed routine extraction.

We have been reluctant to adopt the routine procedure and have resorted to breech extraction only when indicated. However, indications have been broadened considerably and, at different periods covered by this report, from 35 per cent to 65 per cent of cases have been delivered by breech extraction. We believe that further trial by experienced obstetricians is indicated.

Episiotomy.—In our experience, maternal morbidity in breech presentations can be expressed largely in terms of severe perineal damage and we believe almost routine episiotomy is indicated, not only for the benefit of the mother, but also for the protection of the fetal head and brachial plexus.

Care of Prematures.—Until more is known in regard to the *prevention* of prematurity, more attention to the care of the premature infant, in special nurseries, by trained personnel, will help to lower mortality in this large group of cases.

Summary

The fetal risk in breech presentations is more than with vertex, even in expert hands.

The maternal risk is not increased, and mortality can be explained by associated conditions not concerned with the position of the fetus. Slight increase in maternal morbidity is largely the result of a higher incidence of severe perineal injuries which can usually be prevented by episiotomy.

The very high gross fetal death rate is to a great extent due to the inclusion of very premature infants who would have little chance of survival with any position, of those having severe malformations, and of those who are already dead on admission.

We are unable to find an increased risk for viable prematures when presenting by breech.

Stillbirth and neonatal mortality for term babies is for 1933 to 1937 6.5 per cent, for 1942 to 1946, 3.5 per cent.

There is a definitely added risk to breech babies from prolapsed cord which occurs about six times as frequently as in vertex positions.

Birth weight is an important factor in fetal death for breech babies. Babies of medium size have the best chance of survival when delivered vaginally.

Although it is thought by some authors to be associated with a definitely higher death rate, we were able to show very little, if any, higher mortality for frank breech.

Increased length of labor is not a factor of importance in a higher death rate.

Babies of elderly primiparas with breech presentation have a high mortality rate if delivered vaginally.

Prophylactic version as a method of reducing breech mortality, we believe, deserves more universal consideration.

Elderly primiparas, cases with pelvic contraction, even though of mild degree, primiparas with large babies, and cases with various combinations of these conditions deserve careful consideration of delivery by cesarean section.

Better care of prematures should help reduce mortality among those developed sufficiently to survive extrauterine life.

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Discussion

DR. M. PIERCE RUCKER, Richmond, Virginia.—In the middle trimester of pregnancy, the fetus commonly presents by the breech; consequently, if the patient goes into labor prematurely, breech presentation is frequent. At term, the majority have rotated to a cephalic presentation, unless there is something that prevents spontaneous version. Hydrocephalus and major deformities of the fetus and various degrees of double uterus are common causes of breech presentations. Way, of Newcastle-on-Tyne, is of the opinion that the müllerian ducts fail to fuse completely into a normal single uterus in over 1 per cent of patients and that this is a common cause of malposition. One can see then that breech delivery must carry a high gross fetal mortality, since many fetuses are premature, many have deformities that are incompatible with continued life, and many are born by imperfect uteri. What is the actual hazard of breech delivery, is an important question which Dr. Seeley has undertaken to answer from his experience at the Harper and the Herman Kiefer Hospitals and from a review of the recent literature on the subject. After the prematures, the babies with deformities incompatible with life, and those who were dead before labor began were eliminated, there was a mortality of 3.5 per cent in his five-year group, 1942 to 1947. He is to be congratulated on this low figure, but low as it is, it is 2.4 per cent higher than his general fetal mortality for the same period. In analyzing the causes for this difference, he found that prolapsed cord accounted for 12 per cent of the total mortality. This accident occurred 31 times in 984 cases with viable babies, or 3.2 per cent. When I first read this, I thought that the frequency of prolapsed cords was unusually high. I find, however, that in the past five years I have had eight prolapsed cords in breech cases, which is slightly less than 4 per cent. It just goes to show that impressions are often wrong. In only two instances did the accident have any influence on the fetal outcome. I was surprised to learn that a viable premature had as good a chance of survival in a breech delivery as in a cephalic. My impression was to the contrary, but then again my impression might be wrong. I did not have time to check this one.

The hazard of a breech birth through a contracted pelvis is a well-recognized one. However, it plays no part in Dr. Seeley's series, as there were only 22 patients with contracted pelves and he delivered 70 per cent of them by cesarean section. He had no deaths in this group.

I was quite interested in his table showing the mortality rates in relation to birth weights. Of the babies who weighed between 5½ and 6 pounds, 10 per cent were lost. Of the 6-pound babies, 4.4 per cent were lost, as contrasted with 2.5 per cent of the 7 pounders. When, however, the baby weighed 8 pounds, 11.3 per cent were lost and, of the 9 pounders, 20 per cent were lost. My experience is in accord with this finding.

At the first American Congress of Obstetrics and Gynecology, the subject of breech deliveries was assigned to me. At that time I charted the babies by total length. The fetal loss fell as the total length approached 50 cm., only to rise sharply in the small group of postmatures. Dr. Seeley's experience confirms the general belief that the elderly primipara

is a poor subject for a breech delivery. His fetal death rate in this group was twice that of the young primipara. His figures also show that results are better when the breech delivery is conducted by experienced operators. Nowhere in obstetrics do skill and judgment show to better advantage than in the management of breech presentations.

In the practical management of breech delivery, I am glad that Dr. Seeley emphasized episiotomy. Too much emphasis cannot be put upon this. It should be done in every case. The incision should be wider than you think is necessary and even then it will frequently be too small. This is especially likely to be so if you follow the plan of delivering the baby soon after the cervix is fully dilated. If the birth canal has been properly prepared, the baby should roll out with the gentlest of guidance. Sometimes the cervix will close down on the aftercoming head. When that happens, it is easier to push the cervix up over the head with your fingers than it is to push or pull the head through the cervix. I have never seen this maneuver described, but it has served me well for years.

As to prophylactic version, much can be said on either side. Kellogg lists external version among the causes of premature separation of the placenta and Gibberd in a recent article says that there is no correlation between the force used and the amount of hemorrhage, nor between the amount of hemorrhage and the prognosis for the fetus.

I have studied recently the deliveries for the past four years in the Johnston-Willis Hospital (Richmond, Va.), and the ones that I and my associates had conducted in the same period elsewhere. There were 4,848 deliveries with 223 breech presentations or 4.6 per cent. The gross fetal mortality was 16 per cent. Thirty breech presentations were in twin pregnancies. There were 193 breech presentations in single pregnancies, and of these 31 babies were lost. Twenty fetuses measured less than 40 cm. In other words, 20 mothers did not reach the stage in which external version is even considered. Eleven were possible candidates for external version. Of these candidates, four had babies measuring 41, 42, 42, and 46 cm. total length, and weighing less than 2,500 Gm. Had external version been attempted on these mothers, the question would naturally have arisen, did the manipulation cause the premature labor? Two mothers were toxic and had stillborn infants, and it was thought that the result would have been the same regardless of the method of delivery. There were two cases of hydrocephalus and one of these in addition had a spina bifida. In one case there was a prolapsed, pulseless cord when the patient was first seen, and the baby was macerated. In the two remaining fetal deaths hemorrhages into the suprarenal capsule occurred. Since this lesion is twenty-two times more frequent in breech deliveries than in cephalic presentations, it is fair to say that it would have been better had these babies been turned prophylactically. On the other hand, among the 4,848 cases, there were eight external versions. One of these babies had convulsions but apparently recovered completely. One baby was lost. The mother had a bicornate uterus. External version was performed twice. Two days after the second version the mother had a hemorrhage. Shortly afterwards she went into labor and had a stillborn infant measuring 48 cm. There was a low-lying placenta. Whether the manipulation caused the bleeding or not, I cannot say. Had I been wise enough to have done an external version on the two cases that had hemorrhages into the suprarenal gland and to have refrained from doing it on the patient who proved to have a bicornate uterus, I might have saved three babies.

I believe that external version is especially indicated when there is any question of disproportion. If the head can be gotten into or above the superior strait, you can better judge the relative size of the fetal head and the maternal pelvis. Roentgen-ray mensuration of the fetal head when it is under the mother's ribs is apt to be very misleading. Someone has suggested that the mother be x-rayed in the prone position so as to bring the head as close to the film as possible. I have had no experience with such a posture, but I do know that a picture with the mother in the supine position is worse than useless.

In conclusion, I would like to ask Dr. Seeley why there were so many more breech cases in his first series than in his second? In 1933 to 1937 there were 773 breech deliveries and in 1942 to 1946 there were only 467. Has he found a way of decreasing the number of premature deliveries? If he has, that would be, to my mind, the most valuable part of the discussion.

DR. PAUL TITUS, Pittsburgh, Pa.—Dr. Seeley's splendid summation of the subject of breech presentation is difficult to discuss adequately because it touches on so many different points of importance. Fetal mortality is the criterion which he has used in judging what is safe and what is dangerous in this complication.

His paper clarifies many points, and leaves others still somewhat unsettled, probably purposely so. For example, he establishes, contrary to a common impression, that pelvic contraction is not a probable etiological factor in breech presentations; that the etiology of this condition is more likely to be fetal than maternal, and that prematurity is one of the chief fetal factors.

He finds from his extensive analysis that frank breech does not increase fetal risk, nor does early rupture of the membranes, except for prolapsed cord. He finds no added risk in attempts at external version if properly done, but in all that has to do with breech presentation he emphasizes, quite properly, that the skill of the attendant is of the greatest importance in accomplishing a minimal death rate. All of this is helpful to an important degree.

Nevertheless, he leaves us undecided on the still debated question of whether extraction should or should not be done promptly after the patient enters second stage. I should like to add only three points to Seeley's comprehensive study and analysis of this subject.

The first of these is approval of extraction of breech presentations promptly after they have entered the second stage of labor. The second is that forceps be used on the aftercoming head except in those, such as prematures, that can be delivered almost spontaneously. The third is that especial gentleness in resuscitation be observed. Sudden compression of the aftercoming head to pass the pelvis brim is probably much more traumatizing and shocking than the gradual moulding of a vertex presentation, so that resuscitation methods must not add to this.

DR. G. D. ROYSTON, St. Louis, Mo.—Dr. Seeley is to be congratulated on his low fetal mortality in breech delivery. There are a few points in this connection that I want to emphasize.

The arcuate uterus may be considered as one of the possible etiological factors and especially so where recurrences are common after external version. Three Kotex pads snugly strapped with adhesive to each side of the abdomen, to narrow the transverse uterine diameter until moderate engagement occurs, usually within one to two weeks, or labor begins, will usually prevent recurrence of breech presentation after external version.

Dr. Seeley's excellent results were obtained by these deliveries being conducted by highly trained experts. The majority of such cases are now, and for an indefinite future will be, delivered by those of less obstetric training, skill, and judgment. Some three years after completing my residency, I delivered three breech presentations in one month, with an infant mortality of 100 per cent. Since that time, I have had a very wholesome fear of this condition. For the past 34 years I have followed the method of Bumm, which is as follows:

a. Do nothing until the posterior buttock is visible at the vulva. At this point the breech and usually one or both thighs alongside have passed through the cervix;

b. Place the patient's hips well over the edge of the delivery table;

c. Give 1 c.c. of pituitary extract intramuscularly;

d. Under light obstetric anesthesia, make a mediolateral episoitomy incision. The great majority of infants will then be quickly and spontaneously born. A small number requiring assistance in delivering the aftercoming head can be easily delivered with the Piper forceps.

Bumm emphasized that all expulsive force should come from above, which uniformly maintains flexion of the head and lessens the frequency of extension of the arms. These latter points greatly determine fetal dangers during delivery, according to Potter.

DR. LOUIS E. PHANEUF, Boston, Mass.—Because of my interest in the subject presented by Dr. Seeley, I had the breech deliveries at the Carney Hospital reviewed for a period of ten years, from July, 1937, to July, 1947. The Service is a combined one, having 62 beds, 33 gynecologic and 29 obstetric. There were 7,200 deliveries with 240 breech extrac-

tions, 220 extractions for breech presentations and 20 extractions following internal podalic version, 3.3 per cent. These were all single breeches, the breech extractions in twin pregnancies being eliminated.

In this series, the shortest primiparous labor was two hours, the longest thirty hours, and the average thirteen hours and 39 minutes. A primipara, 42 years of age, was delivered of a 6 pound, 12 ounce infant, presenting by the breech, after a six-hour labor.

The method of delivery is of great importance in minimizing fetal mortality. We believe that deep surgical anesthesia, a deep episiotomy, a scrubbed assistant, a vaginal speculum to create an airway to the baby's mouth, and the Piper aftercoming head forceps, all play a prominent role in the management of these cases. At the Carney Hospital, we leave our cases to their natural course as long as progress is being made and interfere only when the opposite obtains. In the 220 cases of breech presentation under study, during a ten-year period, cesarean section was performed 13 times, or in 5.9 per cent.

This group of cases, consisting of single breeches in infants of 26 weeks or over, shows that fetal mortality was represented largely by stillborns, prematurity, and nonpreventable causes. The highest mortality occurred among premature infants, intracranial hemorrhage being the major cause of death in this series.

There were 27 fetal deaths in the 240 breech extractions, 11.2 per cent. If we eliminate from these 27 deaths, 3 stillborns, 3 monsters, 2 macerated fetuses and 3 fetuses with congenital defects, a total of 11, there remain 16 fetal deaths, or a corrected fetal mortality of 6.6 per cent.

DR. JOSEPH L. BAER, Chicago, Ill.—It takes courage and skill to undertake the transmutation of statistics into an interesting presentation. Dr. Seeley has accomplished this well. I desire to present some statistics from the Michael Reese Hospital.

Covering a period of fifteen years, we had a total of almost 28,000 deliveries, with an incidence of breech, including all types of infants, of 3.4 per cent. Eliminating all infants under 2,500 Gm., twins, monstrosities, etc., we have a percentage of 2.4.

In the primigravida group, the first stage of labor was under twelve hours in 58.5 per cent and the second stage averaged an hour and twenty minutes. In the multiparous group, the first stage was less than twelve hours in 82 per cent. The second stage averaged only twenty-seven minutes.

The incidence of 2.4 per cent represents 592 breech presentations. Of these, 443 (75 per cent) were frank breech presentations. This is a much higher incidence of frank breech than I had realized.

Analysis of the type of delivery is as follows: in the primigravida group, 185 were spontaneous, with manual aid, 160 were by extraction, and 58 were delivered by cesarean section. In the multiparas, 151 were spontaneous with manual aid, 96 were by extraction, and 16 were delivered by cesarean section. Of the total of 74 cesarean sections, 39 were done because of the breech and 35 were done for other indications. There was no maternal mortality in the entire series.

The over-all fetal mortality in the series of 592 breech presentations was 4 per cent. No fetal deaths occurred in the cesarean section group. Fetal death rate in spontaneous breech delivery was 2.7 per cent in the primigravidas and 2.6 per cent in the multiparas. The death rate in the extraction series was 5 per cent in the primigravidas and 7.3 per cent in the multiparas.

This markedly increased fetal death rate in the group delivered by extraction (double among the primigravidas and triple among the multiparas) is a potent argument against routine breech extraction. If a well-trained and experienced group of specialists cannot avoid such a marked increase in fetal death rate accompanying breech extraction, how can we justify a recommendation for routine breech extraction?

DR. SEELEY (Closing).—Dr. Rucker asked why we had so many more breech cases in the first group. The reason is that they represented deliveries from two hospitals and in the last group most of the cases were taken from the hospital in which we do our private work and the skill of the attendants was greater. That is why the discrepancy shows up in the way it does.

THE USE OF METHIONINE IN OBSTETRICS*

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Montreal, Quebec

(From the Royal Victoria Hospital, McGill University)

THE liver and the kidneys are vital organs in every human being. Of necessity, they must play an even greater role in pregnancy. Consequently when certain complications occur, the essential functions of these organs are frequently found to be impaired.

Experimental hepatic and renal damage in animals has been produced by various methods. Necrotizing nephrosis in combination with hepatic injury has been caused by purely dietary restrictions; these manifestations were similar to those found in the human being where the hepatorenal syndrome occurred.[1] Administration of chloroform, phosphorus, or other chemicals also caused marked liver necrosis. However, these added chemical factors were contingent on the fact that dietary deficiency played the predisposing role in the causation of this damage.[2]

Gyorgy notes the similarity of experimental nutritional necrosis in the kidneys and liver to the pathologic findings in the eclamptic patient. Hypoproteinism is a most frequent finding in both conditions. This protein depletion may be the common factor which renders the liver more susceptible to damage by hepatoxic agents.

Glycogen has been established for many years as a liver and kidney protective. But only recently has protein been proved to play a most important role in the protection of all body tissues. Normal liver and kidney functions can be maintained only when there is adequate protein intake.[3] On account of these facts, the diet in pregnancy should fulfil certain requirements. It must be acceptable to the patient and it should allay hunger. A well-balanced diet is essential relative to protein, carbohydrate, and fat intake. There should be adequate vitamin and mineral content. Sufficient protein should be supplied to replace wear and tear of tissue in the mother and, at the same time, supply the needs of a growing fetus. This does not always take place.

It has been shown that if acute protein depletion does occur restoration of proper levels may be obtained by the intravenous administration of normal or concentrated plasma, protein hydrolysates, or the use of various amino acids.[4]

Our attention has recently centered upon the possible value of methionine as an adjunct in the treatment of certain obstetric complications which have frequently ended fatally. We know that methionine is a very necessary part of the normal diet; workers have estimated that 2 to 5 Gm. is the normal daily

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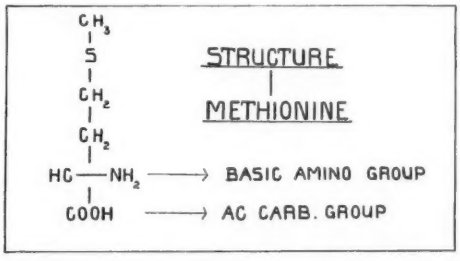
intake for an adult.[3] It is an essential amino acid being provided only from foods and cannot be synthesized in the body. It is chiefly obtained from serum albumin, egg-white and milk.

Amino acids are indispensable for the formation of proteins. In addition, all have specialized individual functions. For example, methionine donates both active methyl and sulfydryl groups. Cystine was once considered to be the essential sulphur-containing amino acid but this place has now been given to methionine. In this case, however, the dispensability of cystine is only relative; if cystine is not provided in the diet, enough methionine must be given to furnish the combined requirements of methionine and cystine to meet the metabolic needs. Methionine also serves as a source of active methyl groups. The quantity required for this purpose will depend upon the availability of other methyl donators such as choline which should also be present in the diet.[6, 7, 8, 9, 10]



In animal experimentation, methionine is shown to be lipotropic, having a favorable influence on the liver similar to the combined action of cystine and choline. Administration of this substance prevents fatty infiltration of the liver. In spite of low protein intake, liver protection is afforded if methionine is given.[3] Miller and Whipple were able to demonstrate the same beneficial effects if methionine were administered to protein-deficient dogs just before or after deep chloroform anesthesia.[2]

We agree that results of experiments in animals do not always coincide with clinical results found in the human being. Nevertheless, treatment of certain complications in obstetrics merits study relative to liver and kidney damage. There is definite clinical evidence that *acute* degenerative changes are beneficially affected by this substance and, though there have been clinical reports to the contrary, the chronic lesions may also be benefited by its use.[11, 12, 13, 14]

Beams and Endicott have recently published their work relative to cirrhosis of the liver in the human being. Severe cases responded well to diet high in methionine content. Results were further improved by a methionine supplement. This clinical improvement was substantiated by liver needle biopsies and histologic examination of the tissues. The study suggests that methionine was responsible for the improved histologic changes in the liver.

Four obstetric complications readily lend themselves to such a study. These are the toxemias of pregnancy, infectious hepatitis occurring in pregnancy, postdelivery shock associated with the hepatorenal syndrome, and hemolytic disease of the newborn. Our observations and results will be divided into four parts.

Toxemia of Pregnancy

There is a tendency to hypoproteinism during pregnancy. Toxemia causes this condition to become more pronounced. Macarthur has shown that hypoproteinemia coincides with increased plasma volume; the resulting protein and hematocrit levels expressed in percentage are practically identical throughout pregnancy. He found that there was a difference of thirty per cent in pre-eclampsia, while in eclampsia the variation was even more striking, with a rise in hematocrit levels and a marked fall in plasma proteins.[15]

It should be emphasized that plasma proteins do not fall until after protein reserves are used from such organs as the liver, kidneys, and alimentary tract.[16] Recent work also shows depletion of muscle and fascia before the blood levels fall.[17] As a direct result of this depletion, the vascular, liver, and kidney functions are impaired. The effects of this impairment act as indicators in assessing severity of disease and prognosis; for example, one considers extent of edema, quantity and quality of urinary excretion, presence of jaundice, or other manifestations of liver impairment.

TABLE I

TOXEMIA CASES: 1944-47

	NO.	MAT. MORT.	FETAL MORT.
PRE-ECLAMPSIA	361	1 (·3%)	44 (12%)
ECLAMPSIA	22	3 (13%)	8 (36%)
NEPHRITIC TYPE	15	0	6 (40%)
ESS. HYPERTENSION	38	0	2 (5%)
TOTAL	436	4 (·9%)	60 (13%)

TABLE II

RELATIONSHIP OF OEDEMA TO PLASMA PROTEIN IN PREGNANCY. SEPT. 1946 – JAN. 1948.

GRADE	TOT. PROTEIN	ALBUMEN	GLOBULIN	A/G RATIO
NO OEDEMA - 14 CASES	6·31			
MILD OEDEMA - 27 CASES	5·77	3·60	2·01	1·79
MOD. OEDEMA - 24 CASES	5·56	3·47	1·91	1·81
SEVERE OEDEMA - 4 CASES	3·73	2·25	1·30	1·73

In our clinic, toxemia of pregnancy occurs frequently. At present, there are more deaths which are attributed to this cause than to any other complication in obstetrics.

Edema is commonly caused by a depletion of plasma proteins as shown by Table II.[16]

All patients included in this table were admissions to our toxemia service. Those who demonstrated normal blood values for pregnancy showed no evidence of edema. This symptom appeared with lowered plasma-protein levels and edema became marked when the total protein blood level fell below 4 Gm. Both albumin and globulin fractions dropped in those toxic cases included in this series; the ratio showed only slight variation and thus could not be considered significant. (Table II.)

Liver function undoubtedly plays a major role in the case of the toxemic patient. Estimation of impairment is difficult. Numerous liver function tests have been employed but they are all found wanting in some respect. We are now trying a battery of flocculation tests; for our use the most reliable is probably the cephalin-cholesterol flocculation test. This aims at determining liver deficiency. Though the findings are variable, this test shows in Table III that the liver is frequently affected by true toxemia of pregnancy. It also demonstrates that impairment is more pronounced in those cases which are more severe from a clinical aspect.

TABLE III

CEPH. CHOLESTEROL FLOCC. TEST IN PREGNANCY.
JAN. 1947 - MARCH 1948

DIAGNOSIS	TOTAL CEPH. DONE	TOTAL CEPH. NEGATIVE	TOTAL CEPH. POSITIVE	% POSITIVE OF TOTAL
HYPERTENSION	6	5	1	16%
PRE-ECLAMPSIA	20	13	7	35%
ECLAMPSIA	5	3	2	40%
RENAL DISEASE	2	1	1	50%
TOTAL TOXIC CASES	33	22	11	33·3%
NORMALS	31	29	2	6·45%

During the last four years, we have had the same routine orders for toxemia patients in the Royal Victoria Hospital. These orders include complete bed rest, adequate balance of fluid intake and output, and proper bowel management. The diet has been neutral ash and low in salt; protein intake is 110 Gm., plus carbohydrate 275 Gm., and fat 90 Gm. Induction of labor has been initiated when indicated.

Recently, we have supplemented our routine treatment with quantities of whole blood or plasma in selected cases.[18] We have also attempted to evaluate certain protein preparations by mouth and by the intravenous method. Methionine has been used in the severe types of pre-eclampsia and in all eclamptic patients. When possible, this is given by mouth in 0.5 Gm. tablets or crystals dissolved in tomato juice; 5 to 10 Gm. is the usual daily dose. When it is given intravenously, we have used as much as 20 Gm., diluted to a 2 to 3 per cent solution in 5 per cent glucose and water.

There have been seventeen severely toxic patients who received methionine for periods from one to four weeks. They include eight pre-eclamptics, six eclamptics, and three severe cardio-renal cases with superimposed toxemia of pregnancy.

Twelve of these cases were treated in the Royal Victoria Hospital, while five others were under the supervision of J. L. Macarthur in the Montreal General or Catherine Booth Hospitals. Every individual was severely toxic. In

addition, there was some added indication for its use such as definite evidence of hypoproteinism, edema, or oliguria as shown in Tables IV, V, VI.

TABLE IV

PRE-ECLAMPSIA SEPT. '46 - MAR. '48

	NO		ONSET	PARITY	PREVIOUS HISTORY AND PRESENT PREG	A.P. CARE	DELIVERY	FOETUS	CLINICAL FEATURES	MAT. RESULT IN HOSPITAL	FOLLOW-UP
ROUTINE WITH METHIONINE.	4	a	AT 37 WKS	III	1944 NEUROSIS LABILE BL/PR	CLINIC	R.M.I.	2460 gms	XS GAIN IN WT BL/PR 180/130 ALB. ++++ CEPH. FLOC. ++	EXCELLENT DIURESIS BL/PR 145/105 (ON DISCH.)	6 MTH. BL/PR 142/90 URINE - TR. HEADACHES
		b	TWINS AT 37 WKS	I	PROTEIN DEFICIENT DIET	CLINIC	R.M.I PROLONGED LABOUR	2385 gms 3200 gms	XS GAIN IN WT BL/PR 154/110 ALB +++ CEPH. FLOC ++	EXCELLENT DIURESIS BL/PR 120/70	3 MTH. NO Cx. BL/PR 98/60 URINE NEG.
		c	AT 38 WKS	I	ASTHMA ARRESTED TBC.	CLINIC	MEDICAL INDUCTION	3105 gms	6 OLB WT GAIN BL/PR 150/90 ALB ++ CEPH. FLOC. NEG	GOOD OUTPUT BL/PR 150/85	———
		d	AT 28 WKS	I	NEGATIVE	CLINIC	R.M.I + BAG AT 32 WKS	1660 gms	12 LB WT GAIN 4 MTHS ALB. ++ BP 145/100 GOOD OUTPUT CEPH. FLOC. NEG.	A.P. DIURESIS BL/PR 130/85	———
ROUTINE.	20		36-40 WKS - 10 32-36 WKS - 6 28-32 WKS - 3 2ND TRIMESTER - 1 (MOLE)	I - 10 II - 3 III - 2 IV - 1 V - 2 VI 2	RECURRENT TOX. 4 TWIN PREG. 2 FOETAL ABNS. 2 MOLE 1	CLINIC - 12 OUT OF TOWN - 5? POOR OR NONE - 3	SPONT - 10 R.M.I - 8 CAES. SECT. - 1 (CARD. DECOMP.) HYSTERECTOMY - 1 (MOLE)	OVER 2500 gms AVG. W - 14 LESS 2500 gms AVG. W - 4 DEAD-BORN - 1 (TRAUMA) ABN. FOET. - 3	AV. WT GAIN 27 LB MILD TOX - 13 MOD TOX - 4 SEVERE 3	GOOD - 16 RESIDUAL HYPERTENSION 4	11 CASES NO RESIDUAL - 10 HYPERTENSION - 1

Diuresis was the most promising feature following this special treatment.[15] It occurred in some instances a few hours after the first administration, especially when the methionine was given intravenously. In several instances, this diuresis occurred in the antepartum state when there was a failure with other forms of ordinary medication, including ammonium chloride and intravenous glucose solutions. There was also a coincident favorable response in the diminution of edema. With reference to the general correction of the protein deficiency further investigation is necesssary.

The one patient who died was poorly treated. This was not entirely due to our neglect. It occurred when we had just commenced the use of methionine and there were other unfortunate circumstances. She had advanced cardiorenal disease and was six months pregnant when admitted to hospital with severe toxemia. Her condition improved considerably with routine treatment and the use of methionine. After three weeks of therapy she left hospital, signing a "refusal-of-treatment" form. Twelve days later she was readmitted in a critical condition. A cesarean section was performed which was immediately followed by coma, hemorrhagic diastasis, and jaundice. She was treated with repeated blood and plasma transfusions but death ensued forty-eight hours later. Autopsy examination revealed massive necrosis of the liver. We did not use methionine intravenously because, when this case occurred, our knowledge of its action and reaction was most limited.

TABLE V

ECLAMPSIA

	No.		Type	Convulsions Before Rx	Convulsions After	Parity	A.P. Care	Delivery	Foetus	Clinical Liver Tests		Maternal Results
Routine ÷ Methionine	5	a	A.P. at 6 mths,	7	0	iii	MD? Out of town	Bag Induction	Dead-born	Ceph-Floc, neg. Oedema ++++	a	Good A.P. diuresis.
		b	A.P at 9 mths,	3	2	i	Treated in Clinic for Toxaemia	RMI. After 3rd convulsion	3020 gms. Alive + Well.	Ceph-Floc - Tr; Itchy skin. Epigastric pain. Oedema +++	e	Poor diuresis Bl. Pr; 150/115 until D.P.P.V.
		c	A.P. at 8 mths	2	0	i	None	RMI.	1600 gms.	Ceph-Floc ++++ Oligoria - marked Oedema ++		All other cases
		d	Intra-Partum	3	0	i	Good M.D.	Mid-Forceps	3500 gms. Alive + Well	Ceph-Floc. ++++ Oedema +		Rapid diuresis Rapid fall in Bl, Pr,
		e	P.-Partum 4 hrs,	4	0	ii	Good Staff	Twins	2200 g 2000 g Alive + Well.	Ceph-Floc. Not Done Oedema ++++		
Routine Treatment	3	f	A.P. at 6 mths	6	1	ii	M.D. in Malone?	Bag Induction	Lived 2 days	No Liver Function Tests Done		Good diuresis 3 Mths. Follow Up: Bl, Pr; normal Urine Neg.,
		g	A.P. at 8 mths	12	0	i	None	Spont.	Dead-Born Morphine Narcosis?			
		h	Intra-Partum	1	0	i	Poor 1 visit Clinic.	Low Forceps	3210 gms. Alive + Well			

TABLE VI

CARDIO-VASCULAR RENAL DISEASE WITH PREGNANCY-METHIONINE Rx

	ONSET	PAST HISTORY	PRESENT PREG.	DELIVERY	FETAL R.	MATERNAL RESULT.
a.	24 WKS	SCARLET FEVER WITH NEPHRITIS T-ECLAMPSIA T-SEVERE PRE-ECLAMP	BL/PR. 195/105 ALB ++++ CASTS ++ OEDEMA + CEPH. FLOCC. ++	SPONT AFTER 10 DAYS Rx	PREVIABLE	BL/PR 150/90. GOOD DIURESIS 3RD DAY - METHIONINE Rx
b	INITIAL CLINIC VISIT AT 26 WKS	T-PREMATURE-DIED T-BIRTH INJURY III-1938 - A and W OCT. '44-HYPERTENSIVE C-Vs. DISEASES	BL/PR. 220/120 ALB. ++++ FUNDAL : GES. OEDEMA + BL/PR. (2 WKS) 240/120 ALB. ++++ OEDEMA ++++	CAES. SECTION AT 32 WKS.	1100 GMS. A and W	POST-OPERATIVE : GES. SHOCK → (PLASMA BLOOD HYPERTONIC FLUIDS) → BL/PR. RECOVERY. OLIGURIA + JAUNDICE DIED - 48 HOURS
c	?	? ? PARA. XII HEADACHES - 2 YRS DYSPNOEA - 2 YRS	? ? POST-PARTUM ADM. OEDEMA ++++ CEPH. FLOCC. ++++ LIVER AT UMB. ⊙	UNATTENDED HOME DELIVERY	A and W	POST-PARTUM : GES. SHOCK → (PLASMA BLOOD HYPERTONIC FLUIDS) → BL/PR. RECOVERY. RT. HEART FAILURE. OLIGURIA + JAUNDICE — METHIONINE Rx RECOVERY.

All other cases indicated a beneficial result with the use of methionine. However, it is realized that this toxic series is far too small a number from which to make conclusions.

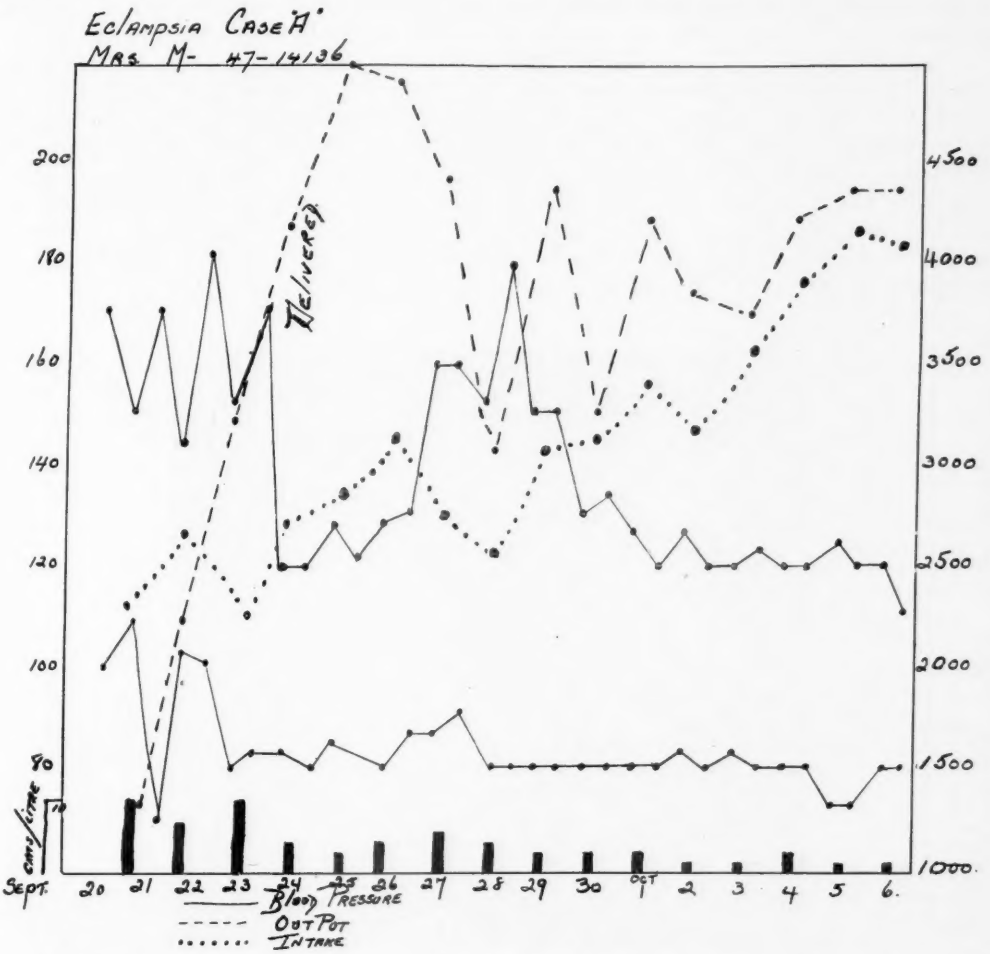


Fig. 1.—Eclampsia, methionine. This patient had recurring convulsions for two weeks in a small hospital. Diet was low in salt but also low in proteins. On admission she was in a comatose state and showed marked edema with oliguria. Daily intravenous methionine was given, 20 Gm. in 2,000 c.c. glucose and water. Note the urine output was far in excess of fluid intake preceding and during labor. Edema was practically absent at time of delivery. Albuminuria was 10 Gm. per litre the day after admission.

Infectious Hepatitis in Pregnancy

This condition has been found to be more serious in pregnancy due to the fact that acute liver damage is more prone to occur and residual cirrhosis is more frequent than in the nonpregnant individual. We have had three cases where methionine was used. Ten Gm. were given each day in conjunction with 5 Gm. of choline for the express purpose of liver protection referable to prevention of necrosis or cirrhosis. In no instance was the course of the disease shortened, but all three patients progressed favorably with no apparent residual damage.[12] One case was seven months pregnant when the jaundice appeared. She delivered seven weeks later with no toxic manifestations nor any increase in blood loss at the time of delivery. The other two cases occurred in the first trimester of pregnancy and both individuals are awaiting delivery.

Hepatorenal Syndrome

Active therapy is most necesssary in any case of postdelivery shock. Many women who develop obstetric shock with persistent hypotension have been allowed to progress to jaundiced and anuric states without active measures being initiated.

Shock should be treated with plasma.[18] Blood loss must be replaced by whole blood, and methionine should be given intravenously in a glucose solution to aid the plasma in preventing edema, anuria, and the consequent kidney and liver damage. Four cases have been treated in such a manner during the last eighteen months. Whole blood and plasma were given in adequate amounts and this was supplemented with 10 Gm. of methionine given intravenously in 500 c.c. of glucose and water. If indicated, this was repeated in 12 hours; one woman received 30 Gm. in 24 hours with no apparent ill-effects. Repeat doses were given by mouth for several days.

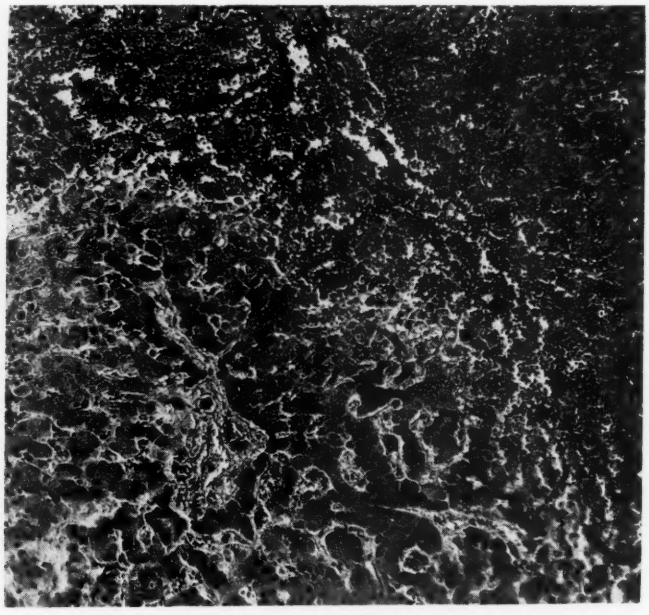


Fig. 2.—Liver in toxemia of pregnancy. Sections of the liver show large, irregularly arranged areas of hemorrhagic necrosis in which the parenchymal elements give evidence of various stages of destruction from simple necrosis to disintegration with extensive hemorrhagic extravasation. This section of liver damage is very similar to those published by Gyorgy, where experimental hepatic necrosis was caused by protein deficient diets.

All cases treated had the typical picture of the so-called hepatorenal syndrome; persistent systolic pressure under 100 with occurrence of anuria and jaundice. The complicating factors in these cases were:

(1) Abortion with hemorrhage and anesthetic shock.
(2) Elderly primipara with three-day labor and postdelivery shock
(3) Placenta previa with massive hemorrhage and subsequent disruption of wound.
(4) Severe cardiorenal disease with postpartum hemorrhage.

These four cases all fall into the group which previously would sometimes progress to cortical necrosis of the kidney or acute yellow atrophy of the liver. Every case survived under the described management.

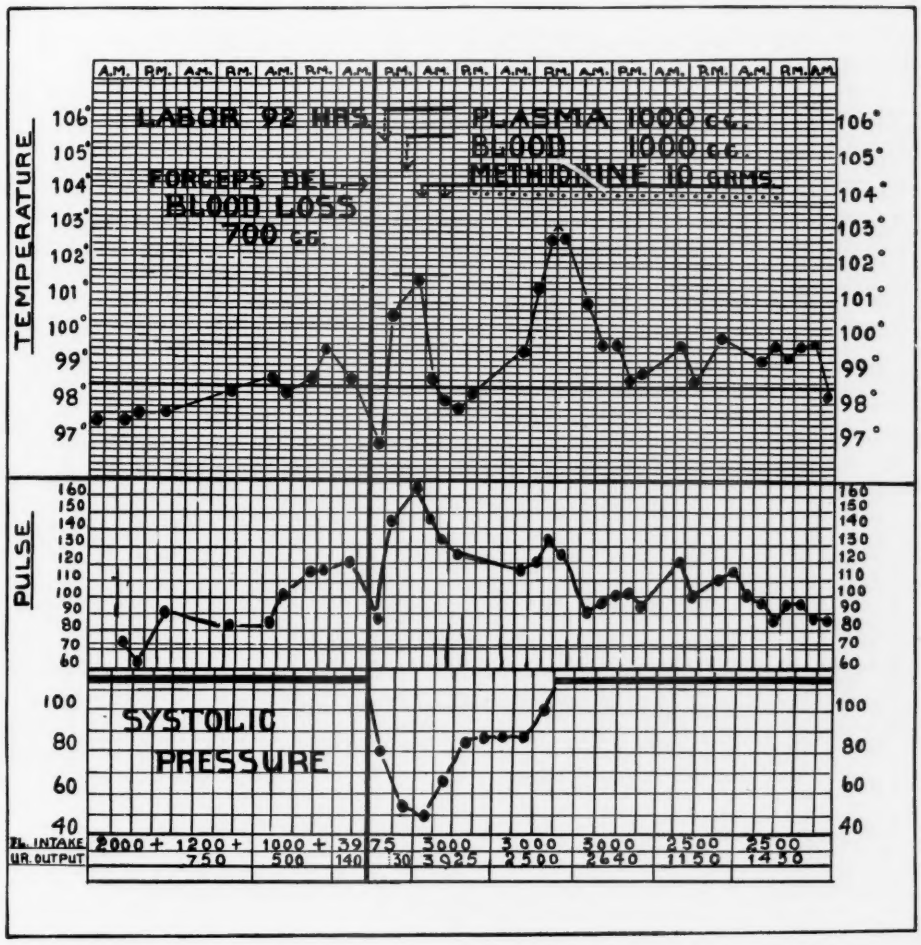


Fig. 3A.—Hepato renal syndrome. This patient had 92 hour labor and difficult forceps delivery. Antepartum dehydration was accentuated by 700 c.c. blood loss post partum. Shock occurred two hours later with the subsequent hepatorenal syndrome. Note the elevated temperature, increased pulse rate, and marked depression of blood pressure. Anuria was present for eight hours. Urine output was observed by means of retention catheter for five days post partum.

Methionine in the Treatment of Erythroblastosis

When the pathologic processes involved in hemolytic disease of the newborn were studied from the clinical and postmortem material, it was obvious that fetal damage to the liver in varying degrees was present in every case.[19] This damage, when once sustained, was thought to be very long lasting, as shown by the follow-up on our own cases and by the work of R. J. Drummond and A. C. Watkins in England.[20] They showed that the liver damage in young persons who were thought to be suffering from idiopathic congenital cirrhosis of the liver was in fact due to the late effects of erythroblastosis due to Rh incompatibility. Taking these facts into consideration, it seemed reasonable to attempt the protection of such fetal livers by the use of methionine whose action as a liver protector had been the subject of so much recent investigational work.[21]

Judging from the available data on daily requirements, an arbitrary dosage of 5 Gm. daily of the crystalline methionine was given, in tablet form to each mother as soon as the first signs of immunization to the Rh-factor was detected

on routine ante-natal examination. This was considered to be greater than the normal maximum daily requirement of the pregnant woman. Such a dose would provide a therapeutic systemic concentration sufficient to deal with moderate liver damage. No attempt was made to assess the woman's daily consumption of methionine in her foodstuffs and any she so obtained was regarded as a supplement.

	CLINICAL	12 HRS	24 HRS	48 HRS	72 HRS		8TH DAY
POST	COMA	SLIGHT	SEVERE	±	0		0
PARTUM	JAUNDICE	0	+++	++	+		SLIGHT
PROGRESS	DYSPNOEA	+	++	+	SLIGHT		0
	LABORATORY						
	HGB.	68	74	76	77		75
	PROTHROM.	36"	34"	27"	23"		16"
	TOTAL PROT.		4·8	5·1			5·6
	CO_2	30	36	47	39		48
	N.P.N	39	51	46	40		38
	CREAT.		4·4	3·3	2·6		1·2
HEPATO-	BILIRUBIN DIRECT		4·	2·7	1·7		·6
-RENAL	INDIRECT		5·9	4·	2·4		·8
SYNDROME	CEPH. FLOCC.		+++	++++	++		+
	THYMOL T		0	0	0		0
	THYMOL FLOCC		0	0	0		0
	F.C. SUGAR		90				72
	ALK. PHOS.		15·2				
	KETOSTEROIDS						1770
	URINE ALB.	2GRS	4·	2·	·5		0

Fig. 3*B*.—Clinical and laboratory findings, in the case of hepatorenal syndrome, as shown also in Fig. 3, *A*.

It was assumed that in the normal course of fetal development, as the need for methionine was manifested in the fetus, then the positive balance available in the maternal organism would be drawn across the placenta by the fetus. This is in accord with the generally accepted and proved theory of fetal demand and maternal supply. Since methionine is an essential amino acid, its passage across the placenta would be uninhibited.

When receiving methionine, the mothers were seen every two weeks before the birth of their babies. A constant check was made on their consumption of the drug and on the antibody blood levels. No case of idiosyncrasy or untoward reaction to the drug was noticed and no patient had to discontinue taking the drug because of nausea. The only complaint was of the tediousness of having to take ten fairly large tablets day after day. In some cases, treatment was for more than 150 days, a total of approximately 1,000 Gm.

The clinical material and controls were selected by discussing the problem of the unborn baby's chances of survival with the mother when her blood first showed antibodies. Most of the mothers in the severer groups could easily appreciate the facts. Excepting three patients who had been severely immunized by recent blood transfusion, all others had experience of previous fetal catastrophes, such as erythroblastotic babies, or babies born dead as a result of the disease. In the milder stages, Groups 1 and 2 (Primrose, van Dorsser, and

Philpott[21]), the use of methionine was not pushed as we were confident that the babies would do well without treatment. However, quite arbitrarily, one case was selected in Group 1 and three in Group 2 and the others used as controls.

When it was obvious that any case was going to fall into the more serious Groups 3, 4, or 5, a most intensive effort was made to talk the mothers into taking methionine with the assurance that we hoped by this means to obtain for them a live baby. All clinic cases were offered the chance but in each group a certain proportion could not be so persuaded; these cases, together with a few private patients whose doctors chose to carry on with observation of their titrations but without methionine, formed a convenient source of controls. The only other medication given these patients was a ferrous sulfate preparation of iron and a multiple vitamin capsule, both in routine use in our clinic.

All erythroblastotic babies born during the year 1947 and up to May 1, 1948, are included in this experiment and are reported.

Samples of cord blood from the liveborn group were examined and the presence of hemolytic disease of the newborn, by our criteria, was confirmed. The deadborn group were subjected to careful pathologic examination and the nature of their disease was studied.

Further cord blood was examined by a battery of liver function tests as a routine. The pediatricians in charge of the cases recorded their clinical findings at birth. Each baby was examined by at least two pediatricians, and at no time before examination did they know whether a baby was a methionine case or a control. Of the liver studies available, only the cephalin-cholesterol flocculation was consistently affected in the severe cases.

Within the limits of the quantity of material available, 45 cases, the original premise is considered vindicated as shown in Table VII.

TABLE VII. HEMOLYTIC DISEASE OF THE NEWBORN

CONTROL CASES AND THOSE IN WHICH METHIONINE WAS ADMINISTERED TO MOTHER AND BABY						
GRADE	CASES	DEAD BORN	ALIVE BORN	SURVIVED	STATE OF LIVER	CEPHALIN-CHOLESTEROL
1.						
Control	10	nil	10	10	Slight to mod. liver enlargement	+++
Meth.*	1	nil	1	1	No liver enlargement	neg.
2.						
Control	3	nil	3	3	Palpable liver and spleen	++++
Meth.	3	nil	3	3	No liver or spleen palpable	+
3.						
Control	3	2	1	1	Liver and spleen enlarged +++	++++
Meth.	4	nil	4	4	Liver and spleen just palpable	+ to ++
4.						
Control	4	4	nil	nil	Advanced erythroblastosis	?
Meth.	3	1	2	nil	Slight liver and spleen enlargement	++
5.						
Control	9	8	1	nil	Hydrops, etc., aborted	?
Meth.	5	1	4	4	Liver and spleen just palpable	++

*Meth.—Methionine cases.

The cases have been divided into grades, and the methionine group in each grade has been compared with the control group. The results are apparent, and the difference between the control group and that having methionine is well seen throughout. Grades 1 and 2 are only mentioned in passing, because no claim is made for any significant difference in the survival rate, although both the clinical and biochemical studies show a significant difference between the two groups. It is in the severer grades, 3, 4, 5, that the difference is most

marked and can readily be seen without the statistical analysis. In these three groups, nineteen control cases had one survivor equalling 5.25 per cent survival. Of twelve cases receiving methionine, ten babies were born alive, and eight survived, giving a gross survival rate of 66.6 per cent.

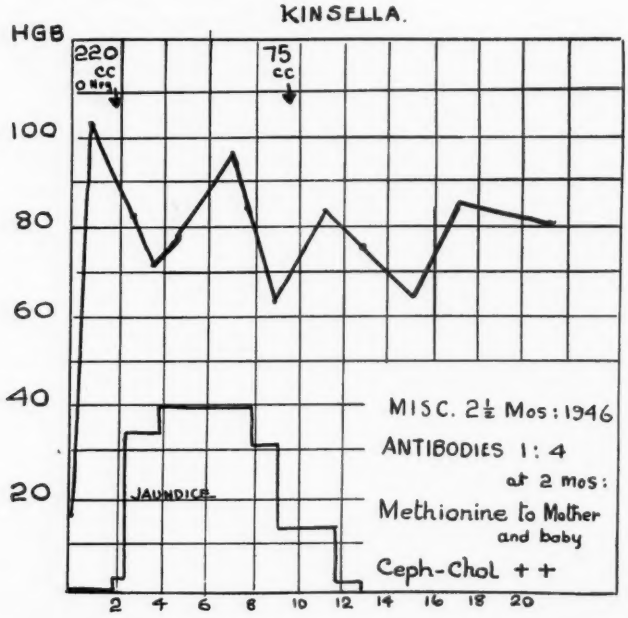


Fig. 4.—Methionine for hemolytic disease of newborn. Mother had 2 previous pregnancies; the first was normal, the second ended in miscarriage. Antibodies were present throughout present pregnancy and showed a 1:64 dilution at 37 weeks. Rupture-of-membranes induction was followed by low-forceps delivery. Mother received over 1,000 Gm. of methionine during four months of pregnancy. Baby received 0.5 Gm. daily for twenty-one days. Blood at birth showed 18 per cent hemoglobin and 1,300,000 red blood cells. Only two transfusions were given, the first being Rh-negative Group O, 220 c.c. whole blood.

In Group 4, the methionine cases labeled as deadborn happened to be twins, which died in utero three days before term. It is interesting to speculate what might have happened if these babies had been induced prematurely or had a cesarean section two weeks before term. The other two babies were born alive and transfused in our usual manner. Both apparently did well for the first three days but one died on the fourth day of atelectasis, and the other died on the sixth day of pulmonary hemorrhage.

In Group 5, the survivor in the control group was Rh negative, but died before leaving hospital of multiple congenital defects. In the methionine group, the deadborn case happened in a woman who had had three previous erythroblastotic babies, all deadborn. She came to us for antenatal care, being four and one-half months pregnant. At this time she showed a fairly high antibody titration. She was immediately placed on methionine, but the damage had been done. She aborted three weeks later of a deadborn macerated fetus.

It should be emphasized that in this disease we are using methionine purely as a liver protective. We know that antibody development occurs as usual in the mother and hemolysis of the red blood cells occurs in the fetus. Our point is that we can treat severe anemia in the newborn but we cannot adequately treat a severely damaged liver.[22] One baby in this series had a hemoglobin of 18 per cent and a correspondingly low red-cell count but responded well to transfusion treatment because the liver was not severely damaged; the cephalin-cholesterol test showed only minor impairment.

All babies who have hemolytic disease receive 0.5 Gm. of methionine daily for at least the first twelve days of life. This is given in doses of .125 Gm. in 5 per cent glucose saline or in the milk. Practically all the babies have taken this mixture with avidity, almost denoting that they required it in their systems.

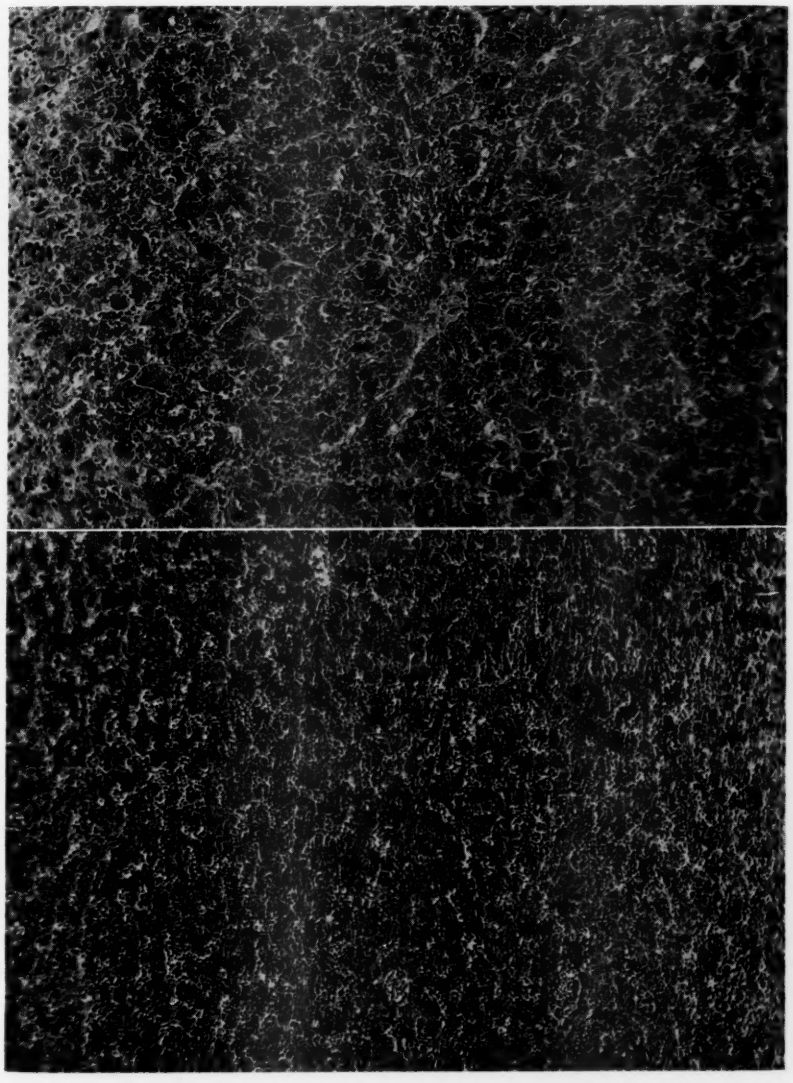


Fig. 5.—Comparison between liver sections from autopsies in erythroblastotic babies where the mothers had high antibody titrations during pregnancy.

Reactions to Methionine

In prescribing any new substance one should be inquisitive with reference to possible reactions. In this instance it is especially true, due to the fact that some protein hydrosalysates given intravenously have produced adverse reactions. Many cases have complained about the size of the pill and some about the taste. We have found tomato juice the best vehicle when methionine is given by mouth. In intravenous use, the crystals tend to precipitate if left standing any length of time or if the solution is more concentrated than 3 per cent. Our procedure is to mix and autoclave 10 Gm. in 200 c.c. of distilled water; this is then added to 300 c.c. of 5 per cent glucose solution.

We have heard unofficially of occasional embolic reactions supposedly from these precipitated crystals. It has not happened in our institution. One case of the hepatorenal syndrome showed a severe reaction to the massive use of plasma plus methionine, from which one learns a great deal. She had been anuric and was markedly edematous. By administering large doses of plasma plus methionine too much fluid was withdrawn from the edematous tissues before an outlet was obtained by increase of urinary excretion. Right-sided heart failure and pulmonary edema were the result. This condition was relieved by the use of ouabain and the fact that diuresis occurred soon after, the patient excreting 2,430 c.c. in twelve hours.

Conclusions

1. Studies in the use of methionine have been carried out in four obstetric complications.

2. The results have been most promising but not conclusive. In the treatment of toxemia and hemolytic disease of the newborn, it is a valuable adjunct to other proved types of therapy.

3. The hepatorenal syndrome can be best treated with the combined use of plasma, whole blood, and methionine.

4. This investigative problem merits further study.

We wish to thank Dr. J. L. Macarthur for contributing the five toxic cases in this series. Thanks are also extended to Dr. J. S. L. Browne and Dr. Martin Hoffman for their cooperation relative to liver function tests.

The methionine used was kindly supplied by John Weyth & Brother (Canada).

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Discussion

DR. L. M. RANDALL, Rochester, Minnesota.—Modern physiologic concepts indicate that a liver containing adequate stores of glycogen, protein, vitamins, and normal amounts of fat,

and which can maintain these stores, manifests the greatest resistance to toxins. These concepts also indicate that after hepatic disease is established an increased intake of carbohydrates and protein is necessary to maintain the stores in the liver and promote regeneration. Thus, the fundamental principle of prevention and treatment of liver disease is to supply these substances in an adequate diet, or by tube feeding or parenteral administration when necessary. The essayist has emphasized the value of an adequate, well-balanced diet in pregnancy. I believe, in general, the average recommended diet is too low in protein and that more protection would occur if greater amounts of protein were included in the diet during pregnancy.

The value of methionine, one of the essential proteins in the treatment of liver disease, has been subject to considerable controversy. Equally reliable authors disagree. The work of Beams and Endicott, in cases of chronic liver disease, based in part on microscopic studies of liver tissue, must be considered significant. The known functions of the liver are many and interrelated. The seriousness of liver disease seems to depend upon the impairment of metabolic activities. One of the difficulties in the interpretation of the results of therapeutic trials in liver disease in general is the suitable criteria for comparison. In individual cases, there often appears to be a variable relationship between clinical and biochemical findings. The results of the tests, as reported by the essayist, are examples.

The flocculation tests, such as the cephalin-cholesterol, depend on alteration of plasma proteins. The essayist presents estimations of the amounts of plasma protein in thirty-five patients experiencing edema and shows no great reduction except in four cases with marked edema but he does not give other components of their examination. Flocculation tests were performed on 25 patients, experiencing either pre-eclampsia or eclampsia, of which 35 per cent were positive. I would like to inquire whether he has demonstrated a correlation between the results of these two tests?

The information concerning the use of methionine in infectious or serum hepatitis, an example of a relatively acute condition, is at considerable variance. The recovery rate is sufficiently high to preclude definite conclusions as regards such specific treatment.

The treatment of shock is primarily one of prevention and, if it occurs, the immediate administration of parenteral fluids. Cannon's definition of shock will fit any condition regardless of cause and, aside from supplying red cells if hemorrhage is concerned, the need is to restore volume of circulating fluid and not for any specific protein, as methionine. Naturally, if a patient is allowed to remain in shock, certain reactions can occur and such specific treatment may be of value.

The employment of methionine in the prenatal period, where evidence of Rh sensitivity exists, deals with 28 patients and within the limits of such a small series the results are encouraging but, as the essayist states, will need further study.

This paper is a preliminary conservative statement from a man with an inquiring mind who enters a very complicated field. He should be commended and encouraged. I may close with a statement made by Dr. F. C. Mann, whose investigations of the behavior of the liver are well recognized, "The known functions of the liver are but part of the physiologic processes involving other organs and tissues of the body."

DR. F. H. FALLS, Chicago, Ill.—The function of the liver is of paramount importance in the physiology of the pregnant woman. The increased metabolic activity seen during pregnancy, the need to meet extra nutritional demands imposed by the developing fetus, and the activity of the placenta throwing into the maternal blood end products of protein metabolism which demand detoxification before their excretion by the kidney, all impose an additional burden upon the liver. When present in abnormally great amounts, these toxins act deleteriously on the liver cells and produce a toxic hepatitis which is reflected by decrease in the liver function as measured by certain tests and by histologic changes seen in the liver of women dead of these toxemias.

Methionine, choline, and cystine are lipotrophic substances and have been found to be useful in the treatment of dietary and cirrhotic fatty degenerative changes in the liver. Normally, an adequate supply of methionine, choline, and other lipotrophic substances permits of a utilization of the fat and prevents its deposition in the liver cells leading to changes

in the reticular structure and cirrhosis. When cirrhosis associated with fat deposition in the liver occurs, it has been demonstrated in human subjects, by taking repeated living biopsy specimens, by measuring the liver function by the thyroid turbidity, cholesterol flocculation, serum alkaline phosphatase, change in the albumin-globulin ratio, and serum bilirubin, that treatment with lipotrophic substances lessens the fatty deposits in the liver and produces clinical improvement and improvement in the liver function as measured by these functional tests. However, this is thought to be the only value of methionine and these lipotrophic substances as far as liver damage is concerned. They have been tried in other forms of toxic hepatitis and experimental toxic hepatitis in anemias and have been found to be of little or no value.

There are several points in Dr. Philpott's paper which need further elucidation. Does he agree with Gyorgy that the lesions in the liver in eclampsia are the same as those found in nutritional necrosis? My feeling from autopsy material which I have studied inclines me to the view held by the older writers that the lesion is primarily periportal and associated with portal thrombosis and, further, that an important group of cases show no demonstrable changes in the liver as measured by the gross or microscopic picture.

It is also necessary to explain why it is that patients on an adequate protein diet still develop this toxemia and that the disease almost disappeared toward the end of the first World War in Germany and Austria when the women were on a very limited protein diet.

In the last twenty-seven years, we have treated our pre-eclamptics and eclamptics on a markedly restricted protein diet with the result that convulsive eclampsia and death from this disease has almost disappeared. Our patients are put at bed rest and given 1,000 c.c. of milk and this is continued until it is evident that the toxemia is controlled or that this regime will not control the toxic symptoms. Only a small percentage fail to respond, if not of the fulminating variety. Our series now consists of nearly 1,400 cases.

Dr. Philpott has properly pointed out the unsatisfactory status of liver function tests, and this, when combined with the rather small number of severe eclamptogenic toxemia cases reported here (17), makes him hesitate to draw sweeping conclusions.

It would seem from the reports in the literature that methionine has been of no value in acute infectious hepatitis and the results in the three cases here reported are inconclusive.

The value of this agent in combating shock seen in the hepatorenal syndrome can only be determined by its use in a large number of cases and by its use in alternate cases. I may say that in these cases I am especially careful to avoid the use of whole blood, especially when the patient may be of the pre-eclamptic group. I have seen fatal anuria develop days after the shock was controlled, even when the blood was carefully cross-matched and typed. Of course, in the presence of severe postpartum hemorrhage as in the case cited by Dr. Philpott, one has no choice but to use blood. The use of methionine in erythroblastosis as a prophylactic measure to protect the liver and permit the fetus to combat the anemia and jaundice of the first few days of life is logical if continued use shows that it will produce the results here reported.

It should be distinctly understood that this paper is in the nature of a preliminary report. Observations are carefully made of the use of a new substance in the treatment of several of the severe complications of pregnancy. This is the only way that information of a reliable nature can be acquired. We are indebted to Dr. Philpott for blazing the trail in this connection.

DR. PHILIP F. WILLIAMS, Philadelphia, Pa.—From a previous review of this subject, I was interested to find out how much methionine could be obtained by a moderately high protein diet. From several sources, Block and Bolling's, and Sahyan's books on amino acids and a number of journals of chemistry and nutrition, I have filled in, as far as possible, the calorie, protein, and methionine content of a diet quoted in Sahyan's book.

Sahyan suggests an intake of 1.9 Gm. as minimal and an intake of 3.8 Gm. as optimal to protect a 70 kg. man. In chick growth studies, these intakes are apparently synonymous

with the terms essential and replaceable. Macarthur has recently quoted Gyorgy to the effect that the prevention of hepatic injury in human beings may be accomplished by an intake of from 2 to 4 Gm. of methionine, or a protein-rich diet with a high methionine content, and mentions that the fat in such a diet should be limited. The methionine content of the diet shown is approximately 33 per cent above the optimal daily intake of methionine for men. For a 56 kg. woman, such a diet should have a high protective value.

It would necessitate the ingestion of ten quarts of milk to obtain 10 Gm. of methionine. In order to obtain an additional 6 Gm. of methionine, a diet would have to be increased by at least two pounds of meat and three quarts of milk daily. The ingestion of such large amounts of food would seem to be out of the question for the average individual. I noted also in my research on the question of methionine content of the edible portion of various foods that chicken muscle ranked next after whole egg, while muscle meats, beef, pork, and lamb, were slightly lower and almost equal; the gland proteins, liver, kidneys, and sweetbreads have a lower content. Rice and shellfish muscle equal lean beef in value.

It is probable that chronic hypoproteinemias in pregnant women cannot be overcome when symptoms of toxemia arise, but if, from the very onset of pregnancy, an effort is made to have pregnant women ingest 100 Gm. of protein daily they will certainly receive an optimal protective intake of methionine. The cystine (dispensable amino acid) content of the diet should always be borne in mind, in regard to the total sulfur-containing amino-acid requirement, because of its sparing action on methionine.

DR. PHILPOTT (Closing).—The chief purpose of this essay is to provoke more interest in liver and kidney function relative to those obstetric complications previously mentioned.

Dr. Randall has asked if there is any correlation between the results of the cephalin-flocculation tests and the progress of the patients. This was certainly true in those babies with hemolytic disease. The babies who died or who had clinical evidence of severe damage all showed four plus cephalin-flocculation tests. In pre-eclampsia and eclampsia, the tests were certainly of value to demonstrate liver damage in the majority of cases, but there were a few who were clinically ill but who showed only plus one cephalin-flocculation, which we consider within normal limits.

In addition, one chart noted that some apparently normal pregnancy cases showed positive cephalin-flocculation tests. But this inaccuracy is true of all liver function tests. For example, the toxic patient who died of marked liver necrosis had a cephalin-flocculation test of plus two. The immediate cause of death was hemorrhagic diastasis and yet the blood showed her prothrombin time to be normal. Some people take the prothrombin time as an index of liver function but it certainly was inaccurate in this case.

With reference to Dr. Falls' remark about comparative pathologic findings in animal experimentation and those of eclampsia, most certainly there is some similarity in the widespread necrosis. However, Gyorgy shows that in animal experimentation the necrosis is usually central and midzonal but the cirrhosis is mostly periportal, where one also finds damage most evident in the eclamptic patient.

Dr. Williams and Dr. Falls both were inquisitive relative to ideas of high-protein diet for the toxic patient. I was most interested in hearing Professor Simmonet of Paris in a lecture a few months ago at McGill University. He stated that the toxic patient should have almost no protein in the diet and that carbohydrate should be increased. He referred to the low incidence of toxemia during the war years in Europe and the low intake of animal protein during those years. But that is not the whole story. Those people had diets fairly high in vegetable protein and he neglected to mention the "protein sparing" effect of carbohydrate intake. If carbohydrate is given correctly, especially orange juice and sugar, about three hours after a meal, the protein is spared in its use for wear and tear and it is stored away for future use.

In a minor degree, fat is also a "protein sparer." It does not naturally follow that just because the Europeans had little meat in their diet, there was little protein; vegetable protein has not as high a biologic value as animal protein but it is still protein.

In toxic cases it is most difficult to arrange a satisfying diet which contains more than 100 Gm. of protein. The patient feels "stuffed" after such a meal. We use eggnogs which are fortified with protein, and these are given between meals. It has been suggested that this protein intake is not necessary for the normal individual. I do not think that we should consider a pre-eclamptic patient normal, especially if she is losing 10 Gm. of albumin in the urine each day. It should be replaced.

As I have previously stated, this is a preliminary report and we are experimenting with a problem which has proved to be most fascinating.

BACTERIOLOGY OF THE GYNECOLOGIC AND INVOLUTING PUERPERAL UTERUS*†

H. Close Hesseltine, M.D., and K. Eileen Hite, M.D., Chicago, Ill.

(From the Department of Obstetrics and Gynecology and the Department of Bacteriology and Parasitology, The University of Chicago and The Chicago Lying-in Hospital)

ALTHOUGH it is established that bacteria are regularly present in the postpartum uterus, adequate bacteriologic study has not been made of the involuting uterus; nor have bacteriologic findings been correlated with the histologic picture except in puerperal infection. It has been assumed generally that the normal nonobstetric uterine cavity is bacteriafree. The paucity of information on the bacteriology and histology of the gynecologic and involuting puerperal uteri has stimulated this study. Histologic and bacteriologic findings of eighteen postpartum uteri removed at varying periods from three and one-half hours to 125 days following delivery have been studied. For comparison, 100 nonobstetric uteri were similarly studied.

Review

The earlier bacterial studies on the flora of the various portions of the female genital tract have been reviewed by Kuster.[11] Special credit prior to this contribution may be given to Döderlein,[5] Menge and Krönig,[12] Hallé,[7] Bergholm,[1] Natvig,[13] Wegelius,[19] and others. More recently particular emphasis was directed toward the pathogens responsible for the febrile postpartum courses by Schottmüller,[14] Schwarz and Dieckmann,[15, 16] Harris and Brown (J. H.),[9] Brown (T. K.),[2, 3] Colebrook,[4] Steinhorn,[17] Stone,[18] and Douglas and Davis.[6] Hite, Hesseltine, and Goldstein[10] studied the bacterial flora of the normal and pathologic vagina and uterus of 248 patients. In this group, the bacterial flora, as evaluated by cultural means, of the vagina of normal prenatal patients was similar to that of patients with mycotic and nonspecific vaginitis, but not vaginal trichomonas. A variety of organisms was removed from the postpartum uterine cavity of normal patients, as well as from those complicated by endometritis. The frequency of isolation of bacteria did not differentiate the febrile from the normal postpartum patients and was similar to that of vaginal trichomoniasis. These observations stimulated further studies of the organisms removed from the uterine cavity after delivery.

Material

The nonobstetric uteri removed for various conditions which are explained in Tables I and II were opened in the bacteriology laboratory after sterilization of the surface by searing with a heated spatula. The myometrium was incised and the cavity opened with sterile instruments. Material for cultures was taken by a sharp sterile curette and inoculated into dextrose brain medium and on aerobic and anaerobic blood agar plates. Isolated bacteria were identi-

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†Read at the seventy-first annual meeting of the American Gynecological Society, Williamsburg, Virginia, May 24 to 26, 1948.

fied in the hospital laboratory by the laboratory technician. Every specimen opened in the operating room was excluded from this study for technical reasons of bacteriologic principle. Uteri from postpartum patients were removed for the assurance of sterilization in all but three instances, where hemorrhage indicated the procedure. Postpartum hysterectomy is not the routine procedure to accomplish sterilization at The Chicago Lying-in Hospital. Consequently, postpartum hysterectomy at arbitrarily chosen times should yield bacteriologic and histologic samplings not available satisfactorily heretofore. Since attempts at aspiration by needle puncture through the anterior cul-de-sac were unsatisfactory, and since cultures taken through the cervical canal in the late puerperium could be conclusive only if they were negative, the above procedure was indicated for scientific study as well as clinical management. The obstetric uteri, taken directly from the operating room to the hospital bacteriology laboratory, were cultured in all but two instances in the laboratory by one of the authors (K. E. H.) using both aerobic and anaerobic techniques, as well as by the technician of the hospital laboratory. Following culture, the uteri were sent to the laboratory of clinical pathology for histologic evaluation.

Three of the postpartum patients had hysterectomy to arrest severe hemorrhage. The remaining fifteen patients of the original eighteen puerperal group were seen by one of the senior staff members as well as medical consultants, who agreed upon the indications for sterilizations. Moreover, a senior staff member approved and was present at each of these operations, to obtain the specimen in as unaltered a condition as possible, and for assurance of welfare to the patient.

TABLE I. CORRELATION OF BACTERIAL CULTURES AND PATHOLOGY OF 100 NONOBSTETRIC UTERI

HISTOLOGIC CLASSIFICATION	TOTAL NO.	PER CENT POSITIVE CULTURES	BACTERIAL CULTURES			
			UTERINE INVASION		NO INVASION	
			POSITIVE CULTURES	NEGATIVE CULTURES	POSITIVE CULTURES	NEGATIVE CULTURES
Leiomyoma	45	24		4	11	30
Adenomyosis	6	33		2	2	2
Malignancy	5	20	1			4
Hyperplasia endometrium	1			1		
Other (see Table II)	43	28	3	7	9	24
Totals	100		4	14	22	60

TABLE II. CLINICAL DIAGNOSES AND BACTERIAL CULTURES OF HISTOLOGICALLY NORMAL UTERI*

CLINICAL DIAGNOSIS	TOTAL NO.	BACTERIAL CULTURES			
		UTERINE INVASION		NO INVASION	
		POSITIVE CULTURES	NEGATIVE CULTURES	POSITIVE CULTURES	NEGATIVE CULTURES
Menorrhagia	17		6		11
Prolapse	17	3	1	6	7
Ovarian cyst	4			1	3
Pelvic inflammatory disease	4			2	2
Dysmenorrhea	1				1
Totals	43*	3	7	9	24

*The same uteri classified as "other" in Table I.

Results

The findings deviated somewhat from the expected picture. It will be noted from Table I that, of the 100 nonobstetric uteri, positive cultures were obtained from 26. The uterine invasion refers to curettement, soundings, or radium application preceding the hysterectomy. Thirty-four strains of both aerobic

and anaerobic bacteria, including aerobic and anaerobic staphylococci, non-hemolytic aerobic streptococci, anaerobic streptococci, aerobic diphtheroid rods, *Bacillus subtilis,* and the anaerobic *Bacterium melaninogenicum* and other Bacteroides, were isolated. Positive cultures were obtained from four of eighteen patients who had preceding uterine invasion and in 22 of 82 patients who had not had prior instrumentation. The most frequently identified organisms were diphtheroid rods—9, *staphylococcus aureus* and *albus*—7 each, *Bacillus subtilis* —6, non-hemolytic streptococci—3, anaerobic streptococci—2.

The histologic classification, although rather inclusive, gives conditions present.

TABLE III. RELATION OF THE INTRAUTERINE CULTURES OF 100 HYSTERECTOMIES TO CERVICAL AND ADNEXAL CONDITIONS

TISSUE EXAMINED	HISTOLOGIC CLASSIFICATION	TOTAL NO.	PER CENT POSITIVE CULTURES	BACTERIAL CULTURES			
				UTERINE INVASION		NO INVASION	
				POSITIVE CULTURES	NEGATIVE CULTURES	POSITIVE CULTURES	NEGATIVE CULTURES
Cervix.—	Normal	28	14	2	7	2	17
	Cervicitis	68	28	2	11	17	38
	Malignancy	1					1
	Not removed	3					3
Fallopian tube.—	Normal	73	21	1	15	14	43
	Chronic Salpingitis	10	20		1	2	7
	Not removed	17	35	3	2	3	9
Ovary.—	Normal	72	18	1	17	12	42
	Cysts	14	29			4	10
	Not removed	14	43	3	1	3	7

TABLE IV. BACTERIAL CULTURES AND PATHOLOGY OF 15 POSTMENOPAUSAL UTERI

CLINICAL STATE	TOTAL NO.	INVASION		NO INVASION	
		POSITIVE CULTURES	NEGATIVE CULTURES	POSITIVE CULTURES	NEGATIVE CULTURES
Malignancy	5	1*	3†		1
Fibroid	3			2	1
Prolapse	7	1		4	2

*Radium 35 days before.
†Radium 54, 57, and 80 days, respectively, before hysterectomy.

The histologically normal uteri are appraised by clinical diagnoses for conditions which indicated the hysterectomy. The frequency of positive uterine cultures in these respective conditions is given in Table II. It is interesting that all seventeen patients with menorrhagia had sterile cultures. Perhaps the bleeding may have been a mechanical or physiologic factor contributing to these results, as is suggested by the finding of Hare.[8] However, investigation of this point has not been made. On the other hand, the number of positive cultures in prolapse might be anticipated. A further relation (Table III) of the condition of the cervix, Fallopian tube, and ovary as related to the endometrial culture from the uteri removed in association with these conditions is offered for completion of the study. There is no apparent significance except perhaps in the instance of cervicitis. Although the bacterial culture and pathologic conditions of the fifteen postmenopausal patients (Table IV) is without particular significance, the data are presented for record. There is not a sufficient number with malignancy of the uterine cavity to find whether the apparent relationship is important. The relationship of the bacterial cultures taken from the uterine cavity (Table V) to the puerperal uterine invasion can be evaluated in protocol

system because of the small number of eighteen. This group is listed chronologically by day postpartum of the hysterectomy. Hysterectomy was done primarily for purpose of sterilization, but the opportunity was thus afforded for adequate bacteriologic and histologic study of the uterine cavity. The febrile course that followed in five patients occurred in all within the first 45 postpartum days, and four within 28 days.

TABLE V. RELATION OF THE BACTERIAL CULTURES TAKEN FROM THE UTERINE CAVITY TO PUERPERAL INVOLUTION

CASE	DAYS POSTPARTUM	BACTERIAL CULTURES	REMARKS
C. H.	3½ (hours)	*†	
E. H.	9	†	Febrile postoperative course
M. H.	11	Anaer. Streptococcus*	
L. S.	18	Anaer. Micrococcus Diphtheroids	
V. P.	21		
E. W.	22		Febrile postoperative course
E. B.	25	Anaer. Streptococcus and Bacteroides	Febrile postoperative course
J. D.	29		
J. F.	38		Febrile postoperative course
C. R.	42		
H. G.	45		
T. K.	45		Febrile postoperative course
H. V. D.	52		
P. P.	53		
M. S.	54		
D. D.	68		
S. H.	80	Anaer. Micrococcus	Retained placental tissue
T. McG.	125		

*Cultures taken by laboratory technician.
†Profuse bleeding at time of hysterectomy.

The detailed histologic studies of these eighteen patients will be presented subsequently.

The postpartum uteri include eighteen specimens removed at times varying from three and one-half hours to 125 days after the delivery of the infant. They are fairly well distributed throughout this period and provide excellent material for study of the changes associated with uterine involution. All eighteen patients had satisfactory postpartum courses, but five had febrile postoperative periods.

The negative cultures obtained from the uteri received three and one-half hours and nine days after delivery are in all likelihood correlated with hemorrhage, since results of other studies indicate the presence of bacteria in the uterine cavity in the immediate postpartum period.

The four specimens from which positive cultures were obtained are of particular interest.

Those removed at eleven and eighteen days are uteri in which the placental site is still composed of degenerating necrotic tissue in which leucocytes are present. The leucocytes are found in greater numbers in the one removed at eleven days but are present in both. This would appear to be a type of tissue in which bacterial growth might well be expected. It seems probable from the appearance of these specimens that the majority of uteri removed during the first two to three weeks after delivery will contain bacteria demonstrable on culture.

The third specimen in which bacteria were found was removed at twenty-five days. It, too, shows many leucocytes and large necrotic areas in the placental site. The endometrium away from the placental site is fairly well developed, but many leucocytes are present in the most superficial portions. In some areas, the appearance is that of granulation tissue; numerous capillary-like blood vessels and a dense infiltration of mononuclear and polymorphonuclear leucocytes are present.

The fourth specimen to yield positive cultures was removed on the eightieth day. An explanation for the presence of bacteria is readily available in the presence of a mass of placental tissue still attached to the uterine wall. The villi are hyalinized and a large amount of calcium is present. Between the placenta and the myometrium there is a wide irregular zone of leucocytes. It seems probable that wherever placental tissue is retained complete healing is impossible and bacteria may persist.

Discussion

The ages of the obstetric patients varied from 19 to 39 years. Two were between the ages of 19 to 24, 7 between 25 and 29 inclusive, 7 between 30 and 35, inclusive, and one at 36, and one at 39 years. Three of the eighteen patients had hysterectomies because of hemorrhage. The other fifteen, however, had hysterectomies to put an end to the reproductive career for eight different conditions. Rheumatic heart disease determined the procedure in six patients. Other indications occurred in progressively declining numbers.

It is interesting that anaerobic bacteria were isolated in all four instances. On the other hand, bacterial cultures of the nonobstetric uteri varied considerably, irrespective of uterine invasion prior to the hysterectomy. The bacteria are compatible with spread of growth upward from the vagina. In the uninvaded uteri, cultures of staphylococci and streptococci composed a slight majority over the other organisms. *Bacillus subtilis* is considered to represent contamination. The other types of bacteria have been isolated frequently from postpartum uteri or from the vagina.

The concept that the nonpregnant and uninvaded normal uterine cavity is free from bacteria needs re-evaluation according to the above findings. The presence of these bacteria in the uterus is consistent with obstetric findings, and their source is logically from the vagina. From the previous findings, it is evident that bacteria may remain in the postpartum uterus for a varying period of time following delivery. The persistence of microorganisms in the uterine cavity may be related directly to its placental site, its extrusion, and especially to retained placental tissue.

The obstetric patient has ordinarily been considered noninfectious. Present and previous observations indicate that after delivery the uterine cavity is infected or a potentially infected zone not unlike a draining abscess or cavity. One might use the term "laudable lochia" in comparing the bacterial behavior of the postpartum uterus with what took place in the early days of surgery. Mechanisms influencing the presence of microorganisms in the postpartum uterus have not been determined by this study. One contention could be that certain bacteria have digestive or other action upon the placental site and necrotic tissue remaining in the postpartum uterus. Accordingly, the obstetric patient is only relatively "clean" bacteriologically, as the uterine cavity and lochia in all puerperal patients harbor bacteria actually or potentially pathogenic. Consequently, it would seem that the unknown factors of microbiologic process in relation to recovery and regeneration of the puerperal and the invaded gynecologic uterine cavity can be solved by diligent, thorough, and well-controlled investigations.

Conclusions

Bacteriologic study has been made of material taken directly from the cavities of 100 gynecologic patients and eighteen involuting puerperal uteri following hysterectomy. The bacteriologic findings have been correlated with the clinical and histologic data. Positive cultures were obtained from twenty-six of the gynecologic specimens, and, with the exception of cervicitis, there was no apparent relationship to pathologic conditions of the adnexa or cervix, nor was there correlation with the presence of leiomyomas, adenomyomas, or malignancy of the uterus. Seventeen uteri removed because of menorrhagia failed to yield positive cultures, while, in prolapse of the uterus, bacteria were isolated from nine of seventeen specimens.

The findings in the postmenopausal uterus were not different from those of the menacmic uteri.

Bacteria were isolated from four of eighteen involuting puerperal uteri removed 11, 18, 25, and 80 days post partum. The bacteriologic and histologic findings can be correlated. Two uteri removed early (three and one-half hours and nine days) were bacteriologically sterile, but hysterectomies were performed because of active bleeding, a factor which undoubtedly altered the findings.

The identity of the bacteria is given, and the significance of the results is discussed.

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Discussion

DR. HERBERT TRAUT, San Francisco, Calif.—Problems of bacterial invasion, especially those of the uterus, are difficult to handle precisely. They do not fall easily into categories because of technical difficulties. If one regards the uterus as an area susceptible to bacterial invasion and then studies the flora of pathogenic organisms as they may be demonstrated in the puerperal or nonpuerperal uterus, there will be revealed a variety of invading organisms which would at first glance seem to be quite impressive. To offset this

first glance, we must be aware of the fact that the offending organism is possessed of widely differing degrees of pathogenicity, on the one hand, and that on the other there are subtle and little-understood mechanisms of resistance to pathogenic influences of bacterial origin. So, to speak of the presence of a bacterial agent capable under some circumstances of producing embarrassing clinical evidences is not final. We must eventually devise a scheme whereby we can more adequately evaluate the potentialities for harm that may be inherent in these invaders. We are all aware of the characteristics of the hemolytic type of streptococcus and have learned to beware and to institute drastic therapeutic remedies when its presence has been demonstrated. However, we know much less and need to learn more of the lower grade pathogenic microorganisms, which on occasion can assume potent influences for harm. It is with these factors that Dr. Hesseltine's paper has to deal. He has given us a factual account of a wide experience in nonpuerperal uteri and a lesser one in those following pregnancy. The story he has presented of bacterial invasion of the uterine cavity is impressive. One could wish that we could have as adequate a presentation of the various influences working in the bodies of his patients which made for serious or less significant pathologic damage.

It is necessary to make one point clear. We are on solid, familiar ground, so long as we are dealing only with the characteristics of well-known organisms. In the confusion involved in shifts of potent pathogenicity and ability of the individual to erect mechanisms of defense, we are still lost in quandary as to the full significance of our data. This presentation, though not as conclusive or as extensive as we need, fills in a chink in the mountain of accumulative data which will eventually be most helpful in solving our dilemma.

To be more specific: Dr. Hesseltine has given us evidence that the nonpuerperal uterus is more often invaded by somewhat pathogenic organisms than we had supposed. The chief incidence of this invasion occurred in patients who had an infected cervix or in those who had myomas or adenomyomas of the uterus. This is an important observation because it has a bearing upon therapeutic procedures. To curette or use radium under such circumstances must inevitably lead to a greater than normal incidence of inflammatory reactions and eventual damage. This may be regarded as the principal and most illuminating feature of his presentation.

The number of postpartum uteri studied may be considered to be too small for statistical evaluation. However, consider the difficulties attendant upon such a study. It can be only occasionally that such uteri may be obtained for the sort of scrutiny which he has given them. One might be critical and doubt the indications for the removal of some of the uteri which were included in this report. This would be small and undeserving, for neither you nor I were there to bear the clinical responsibilities for evaluating the situation. We must, therefore, in all professional charity repose confidence in our colleagues and accept this possible criticism as completely sub judice.

The important fact with respect to the puerperal uterus is that it is an infected organ and that, insofar as the data presented can show, it becomes relatively sterile after the twenty-fifth day post partum, excepting in those instances in which there are retained tissues not readily susceptible of exfoliation. In the latter case, the period of uterine return to a state of bacterial freedom may be indefinitely deferred.

In addition, Dr. Hesseltine has given us detailed and interesting data referable to the healing process of the placental site.

DR. GORDON DOUGLAS, New York City.—Dr. Hesseltine has approached and shed some new light on a problem which has long puzzled the gynecologist and obstetrician. The results of his thorough investigations would appear to justify the removal of many uteri, both in the puerperal and nonpuerperal states, when less radical procedures might have achieved the same clinical results. In this particular respect one is reminded of the material necessary for the last contribution of the late Dr. J. Whitridge Williams, which was presented before this Society at its meeting in 1931.

The most remarkable observation in the nonpuerperal uteri was the finding of sterile cultures from the endometrium of patients with bleeding. The organisms isolated are those

which usually do not produce a true septicemia. Leonard Colebrook has shown by "in vitro" experiments that strains of the anaerobic nonhemolytic streptococci isolated from the puerperal genital tract will not multiply, and frequently are not able to survive a period of incubation in fresh defibrinated human blood, clots, or sera. He attributed this finding to the low pathogenicity of the organisms and to the bactericidal powers of the blood. Interestingly enough, reduction of the pH and a diminution of the antitryptic powers of the blood or sera resulted in a luxuriant growth of the same organisms under similar conditions. Furthermore, Colebrook demonstrated such chemical changes in the lochia and felt that the observations were significant in the explanation of the development of puerperal infection. We have frequently found negative cultures from the uterus at the time of cesarean section when bleeding was excessive and infection known to exist. Consequently, I feel that the presence of blood in these uteri may have been responsible for some of the negative cultures obtained. The same explanation may be tenable in some of the instances of negative cultures obtained following "invasion" of the uteri in the bleeding cases.

In connection with the relatively large number of positive cultures obtained when cervicitis existed, I would like to ask Dr. Hesseltine if the endometrium obtained for cultures was located in the region of the internal os (isthmic portion) or higher up, since the source might have a definite bearing on the result obtained at culture.

My experience has indicated that cancer of the endometrium is frequently infected but that the infection depends on the stage of the disease and on the extent of the necrosis and exfoliation. I believe the negative cultures obtained here are quite consistent with our understanding of this disease. They were obtained for the most part many weeks following radium therapy when there might be no necrosis and, accordingly, no infection. I feel confident, however, that this would not be the case if the disease were more advanced.

With regard to the puerperal uterus, Dr. Hesseltine has presented data indicating that the endometrium is sterile after the twenty-fifth day, except when there is retained tissue. Obviously, to obtain more exact information regarding the time microorganisms disappear from the puerperal uterus, more specimens will have to be studied in the early puerperium, particularly between the seventh and thirtieth days.

About fifteen years ago I carried out a number of experiments utilizing different types of apparatus to introduce a tube through the puerperal cervix in order to obtain cultures from the lochia in the interior of the uterus without contamination from the cervix. Considerable time and effort were spent in these studies and it appeared reasonably certain they were uncontaminated by the cervix. Uterine cultures taken by means of a modified Little tube at the same time gave almost identical results and accordingly for this reason and the complicity of the procedure, the method was abandoned. This, in my opinion, proved the value of cultures obtained in this fashion. The method employed by the essayist in correlating the bacteriologic and histologic findings, however, adds greatly to the knowledge acquired. The approach presented might well be utilized in an experimental study of the effects of sulfonamides, antibiotics or other chemotherapeutic agents.

DR. T. K. BROWN, St. Louis, Mo.—Dr. Hesseltine has discussed the bacteriology and histology of eighteen cases in which a postpartum uterus was removed at various times and for various reasons. Twenty per cent of these cases showed positive cultures; in each case the organism was found to be anaerobic in type. Five of these cases had febrile postoperative courses. Because of the wide distribution of these cases during the puerperium (three and one-half hours to one hundred twenty-five days) the histology portrays well the changes during involution. A description was given of the changes in the endometrium, the myometrium, and the vessels as involution progressed. In the control series of 100 gynecologic uteri, positive cultures were obtained in 25 per cent of the cases, irrespective of whether the uterus had been invaded or not. In the cases of prolapse of the uterus, there were positive cultures in 50 per cent. This would seem likely in this type of case, where the cervix is frequently protruding outside of the body and may be somewhat patulous and exposed to contamination.

Cultures taken of the cervix, before the onset of labor, are usually negative except in cases with marked erosion. Before the expulsion of the mucous plug from the cervix, with the onest of labor, the patient's uterine cavity seems to be protected from organisms. However, as the cervix dilates, organisms may enter the uterine cavity irrespective of whether the membranes are present or not. In other words, the membranes do not offer very much obstruction to the invasion of bacteria and intrapartum infection can occur. I recall a case of a labor of approximately eight hours in which the membranes were not ruptured until the delivery of the baby was in progress; nevertheless, the mother had developed fever during this labor, the baby was stillborn, having died during labor. Cultures of the lung, blood, and peritoneal cavity of the fetus gave the same organisms which also caused the death of the mother three days later. The membranes, in this case, offered no protection from infection to either the baby or the mother.

Either during labor, or shortly thereafter, the uterine cavity becomes contaminated with organisms from the vaginal tract over a period of days and this finally is cleared up spontaneously as the lochial discharge diminishes. It is, therefore, important to eliminate all unnecessary trauma to the cervix or lower uterine segment and to limit manipulation as much as possible. One should do all that is possible to maintain adequate drainage. If this is accomplished, the patient will remain afebrile in spite of considerable contamination of the uterine cavity which is shown either by culture or by the odor of the lochia. In some cases, the mere presence of a tampon or sponge allowed to remain in the vaginal tract, will interfere with drainage sufficiently to cause this patient to have fever, and its removal is all that is necessary to allow the temperature to drop to normal. Perhaps a blood clot or a piece of membrane may act in a similar manner by obstructing free drainage from the cervical canal. I agree with Dr. Hesseltine that rather free bleeding from the uterine cavity, post partum, is conducive to a clean uterine cavity as the organisms are washed out. Of course, if hemorrhage goes to the point that anemia develops, then this makes it possible for a patient to become infected more readily, due to decreased resistance to the organisms.

In the study of bacteriology of uteri, postpartum or postabortal, I have divided the organisms found into aerobic and anaerobic organisms and also a mixed group in which both aerobic and anaerobic organisms were present. Aerobic organisms have been found alone in but 8 to 10 per cent of the cases; anaerobic organisms are encountered in from 45 to 50 per cent of such cases. In about 45 per cent of such cases, a mixed group of organisms are encountered, both aerobic and anaerobic in nature, and this is a group that is demonstrating synergism of organisms in these patients as referred to by Dr. Hesseltine in his series. As a rule, the anaerobic group of bacteria is predominant, being present in approximately 95 per cent of the cases, either alone or synergistically with aerobic organisms of various types. Necrotic tissue is suitable medium for the growth of anaerobic bacteria, as the tissue is detached from the normal circulation and its oxygen content is reduced to the point at which anaerobic bacteria can grow very satisfactorily. Such anaerobic organisms, especially the anaerobic streptococci are proteolytic in nature and digest this necrotic tissue causing it to eventually slough off. This proteolytic tendency may also bring about the invasion of thrombi and the eventual spread of the infection through the venous system, provided adequate drainage is not obtained and the uterine cavity cleaned of its debris. The spread, in this manner, brings about the development of thrombophlebitis. Finally, the dissemination of infection from the pelvis to the lung occurs, as is the case in which fatal infection develops.

In a case of postabortal or postpartum uterine infection, we are dealing with a wound infection and must treat it accordingly. I believe that most abortions are incomplete; at least microscopically, and usually some debris remains after the sac is passed. Some of the placental tissue frequently remains after delivery, although it may cause no demonstrable trouble. I have seen small portions of placental tissue retained for some months, causing considerable disturbance in the menstrual history and finally requiring removal before the patient is brought back to normal. In such cases, where placental tissue remains and is contaminated, involution of the uterus is usually delayed.

Dr. H. S. Crossen taught that gynecologic operations should be postponed for anywhere from four months to a year after a delivery or miscarriage because of the possibility

of streptococci being present in the pelvis and the patient not having sufficient resistance to withstand their invasion if operation were done early. This seems to be borne out in Dr. Hesseltine's series of eighteen cases in which five had febrile postoperative courses.

Dr. Hesseltine has mentioned the difficulty in the classification of bacteria found in his series. This is true because of the synergism of the organisms present. Frequently the aerobic and anaerobic bacteria are present at the same time. In the handling of such cultures, as one begins to obtain the pure culture from the original, there is a separation of the organisms and neither one of them grows out well as the isolation proceeds. The anaerobic bacteria grow poorer as the aerobic organisms are eliminated from the culture and, finally, about the time the organism is obtained in a pure state, it is suddenly lost. This is one of the reasons the classification of anaerobic bacteria has not gone further.

I should like to comment on the use of antiseptic vaginal instillations to combat the invasion organisms from the vaginal tract during labor, or subsequently, and also in gynecologic cases preoperatively.

I found that the use of 1 per cent neutral acriflavine in glycerine as an instillation the night before a gynecologic operation and also the morning of operation would sterilize the vagina and there would be less chance of bringing about the invasion of organisms into the uterine or abdominal cavity. Also, healing of the vaginal operative field was greatly enhanced. The vagina can be sterilized overnight by the use of such instillations. Instillation in obstetric cases is in large part responsible for the fact that we have had no deaths from puerperal infection since January, 1932, during which time we have had 32,640 deliveries up to May 1, 1948.

Several years ago, Dr. Carleton N. Price of Washington, D. C., and I made some cultures of postpartum patients in whom instillations had been used. The number and variety of organisms was greatly reduced as compared with cultures taken in cases in which instillations had not been used. Many cases never had any demonstrable growth from the uterus, post partum. Those that were positive cleared up in a much shorter time than one would expect.

In a paper on the "Bacteriology of the Uterus at Cesarean Section," which I presented before this Society in 1939, I concluded with the statement, "Antiseptic vaginal instillations offer a means of preparation of a patient for cesarean section which will: first, largely eliminate one of the most important causes of mortality, infection; second, reduce the incidence of positive uterine cultures obtained (to one-tenth of the incidence found where instillations were not used); third, make it relatively safe to postpone operation to a much later hour in labor; and fourth, lower the indications for the more radical operative procedures." Of course, intrapartum infection may occur and this can only be prevented by the earlier prophylactic use of the instillation.

DR. N. J. EASTMAN, Baltimore, Md.—In Dr. Hesseltine's present paper, as well as in other communications, he has stressed the fact that the postpartum uterine cavity is contaminated and has likened it to a draining abscess cavity. It will be the purpose of my remarks to call attention to the fact that the bacterial flora responsible for this septic state may be altered greatly by the intra-administration of penicillin. The method we have used was devised by Dr. Joseph A. Guilbeau, Jr., of my service. We employ a small tube 3 mm. in diameter over which a finger cot is stretched tightly and tied down at the proximal end. It is inserted and a pointed stylet is used to perforate the rubber over the end. The rubber then snaps back quickly.

Another stylet carrying a tiny piece of gauze is next introduced. This is rotated, withdrawn, and then cultured. All cultures from patients who had had penicillin were subject to treatment with chlorase so that any effect observed represents the effect of penicillin in vivo and not in vitro while being cultured.

All the bacterial work has been done by Mrs. Isabelle Schaub of our Department of Bacteriology. The cultures were taken between 36 and 72 hours after delivery. The results in untreated patients were in no wise different from those reported by other students of this subject and showed that anaerobic streptococci were present in the great majority of cases along with many other organisms. There were only two completely sterile cultures in the patients who had received no penicillin.

The results in the women who had received penicillin in labor were quite different. The amount given was 200,000 units at the onset of labor in the majority of cases. A minority also received 5,000 units after delivery up to the time the culture was taken. Recalling that in the 32 untreated cases we had only two sterile cultures, it is noteworthy that in this group of 54 who had received penicillin, 32 were absolutely sterile. Moreover, if we include as sterile those cultures showing the pleuropneumonia-like organism (which is known to exist normally in the birth canal and is regarded as nonpathogenic) the percentage goes up to 74. Three cultures show the colon bacillus which would not be expected to be affected by penicillin.

The six treated cases in which the anaerobic streptococci were demonstrated were ones in which the penicillin was given only in 200,000 unit doses, and had the penicillin been continued they also might have been sterile. Some plausibility is lent to this supposition in that nearly thirty-six strains of anaerobic streptococci were highly sensitive to penicillin by recognized tests of sensitivity to this organism.

It is not my purpose in making this report to suggest that penicillin be administered routinely in labor, but since these results conform with our clinical experience it seemed worth while to report them by way of saying that the great majority of organisms present in the puerperal uterus, including the anaerobic streptococci, are vulnerable to penicillin. The implications of this statement in regard to the treatment of antepartum and postpartum infections are obvious.

DR. HESSELTINE (Closing).—Pursuant to some of Dr. Traut's comments, we have been interested in the synergistic relations and results from the synergistic pattern and disturbance of the balance. The isolation of the anaerobes as well as the aerobes also follows along with some of Dr. Douglas' references. Our cultures were taken from comparatively high up in the uterine cavity, the incision being made in the corpus proper well up toward the fundus. This technique was developed originally since we did not know how long after delivery it would be necessary to continue the study. Cultures through the cervix have certain technical faults.

Dr. Eastman's reference to antibiotics is interesting. We have a report now ready for publication in which both penicillin and streptomycin were administered for prophylaxis. There was no reduction in the morbidity rate following penicillin therapy under the conditions of our study. On the other hand, the febrile puerperal course was reduced distinctly in those treated with streptomycin. Because of the dangers of streptomycin, this finding may be unfortunate, inasmuch as it may cause misuse or abuse of streptomycin with the development of drug-resistant strains and other hazards.

THE MORPHOLOGY OF THE HUMAN FALLOPIAN TUBE IN THE EARLY PUERPERIUM*

LOUIS M. HELLMAN, M.D., BALTIMORE, MD.

(From the Department of Obstetrics, Johns Hopkins University and Hospital)

SINCE 1941, women who have had eight or more viable infants have been offered tubal ligation at the Johns Hopkins Hospital. This indication is based on the finding of Eastman,[1] confirmed by Yerushalmy et al.,[2] that women of this parity face a threefold increase in maternal mortality over women in the lower parity brackets. Such a program greatly increased the number of sterilizations performed and would have been entirely impractical, because of limited bed facilities, had it not been for the feasibility of immediate and early puerperal sterilization.[3] This procedure has been eminently successful, as will be shown in a forthcoming publication by Vosburgh and Rice which reviews the clinical aspects of this experience.

The present study deals solely with the morphologic findings in the Fallopian tubes from 715 of these sterilizations carried out between January, 1941, and June, 1947. This represents the material from the vast majority but not from all the tubal ligations, because, in a few instances, the pathologic specimens were either lost or were not fit for study. In no instance was the operation performed on febrile patients nor in any case in which the character of the labor or delivery suggested the likelihood that infection might ensue. All these 715 patients, in other words, were believed to be entirely free of any type of pelvic infection, actual or potential. Every effort was made, within the limitations of a busy obstetric service, to carry out sterilization as soon after birth of the infant as possible. The Pomeroy technique under Pentothal Sodium anesthesia was the method of choice for most of the operations. A small portion of the isthmus of both tubes was fixed immediately and submitted to the pathologic laboratory for examination. For the purpose of this study, all these tubes were reviewed and rediagnosed without regard to the previous diagnosis or to the clinical history. The data thus derived were placed on special punch cards and only then were the clinical data added. These cards were then sorted and the various correlations shown in the tables obtained. During the period under consideration, 46 interval sterilizations were performed as well as 35 ligations accompanying hysterotomy. These two series serve as controls where necessary.

Fig. 1 shows graphically the distribution of the cases according to time of operation. Zero days post partum is used to indicate ligation at the time of cesarean section. One day post partum then indicates operation within the first twenty-four hours, etc. All of the lesions described were divided according to degree into mild, moderate, and severe, but for the purpose of this paper these various categories are grouped together.

Acute Salpingitis.—This lesion varied from the mere presence of polymorphonuclear leucocytes in the lumen to marked swelling of the rugae with a dense infiltration of inflammatory cells, as seen in Fig. 2. Only in the most

*Read at the Seventy-first Annual Meeting of the American Gynecological Society, Williamsburg, Virginia, May 24 to 26, 1948.

severe forms was the muscularis invaded and this lesion has never appeared as advanced as in true, full-blown gonorrheal salpingitis. Bacteria could not be demonstrated by stain and there was no clinical correlation between this finding and the occurrence of puerperal fever. Table I shows the distribution of patients whose tubes showed acute salpingitis according to time of operation. It is obvious that the presence of an acute inflammatory reaction in the tubes is in direct correlation with the length of the delay from delivery to operation. While there seemed to be no relationship between this finding and the postoperative course of the patient, nevertheless, the presence of such abnormal tubes late in the puerperium would seem to be one additional factor in favor of early operation.

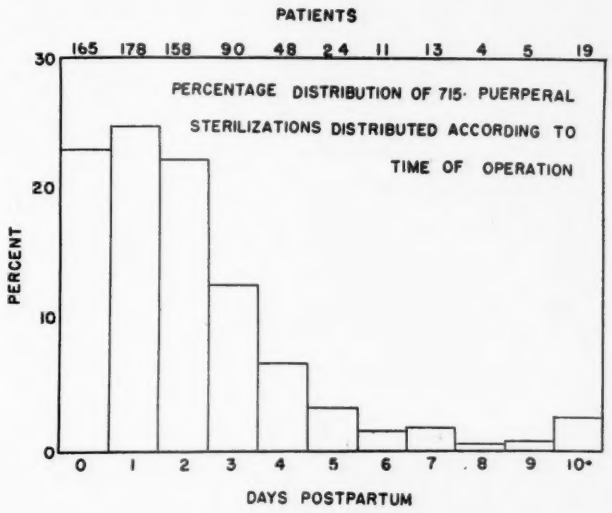

Fig. 1.

TABLE I. THE OCCURRENCE OF ACUTE SALPINGITIS IN 715 PUERPERAL STERILIZATIONS DISTRIBUTED ACCORDING TO TIME OF OPERATION

DAYS POST PARTUM	STERILIZATIONS	SALPINGITIS ONE TUBE	SALPINGITIS TWO TUBES	PER CENT SALPINGITIS
0	165	3	1	2.4
1	178	0	1	0.6
2	158	1	3	2.5
3	90	2	2	4.4
4	48	0	0	0.0
5	24	2	1	12.5
6	11	2	2	36.3
7	13	2	2	30.7
8	4	2	0	50.0
9	5	0	0	00.0
10+	19	2	2	21.0
Control	46	0	1	2.2

Leucostasis.—The pooling of leucocytes in veins associated with diseases where the presence of young white cells are common, such as leucemia, has been recently termed leucostasis. What this means is not clear but such pooling occurs in the presence of young white cells even though the count is not extraordinarily high and it has been suggested by Furth[3] that the stickiness of the young cells in the relatively slow venous circulation may be responsible for this phenomenon. Such a picture is well demonstrated in Fig. 3. Table II shows a

high percentage occurrence associated with the pregnant state, with a definite decrease after the third postpartum day. It is possible that the development of even a mild leucocytosis which sometimes occurs at term and is almost universally present in the puerperium could be responsible for this lesion. It is rare but not unknown in the nonpregnant state and appeared in 8.6 per cent of the 35 hysterotomies.

TABLE II. THE OCCURRENCE OF TUBAL LEUCOSTASIS IN 715 PUERPERAL STERILIZATIONS DISTRIBUTED ACCORDING TO TIME OF OPERATION

DAYS POST PARTUM	STERILIZATIONS	LEUCOSTASIS ONE TUBE	LEUCOSTASIS TWO TUBES	PER CENT LEUCOSTASIS
0	165	17	24	24.8
1	178	15	23	21.3
2	158	12	5	10.8
3	90	6	6	13.3
4	48	1	1	4.2
5	24	0	0	0.0
6	11	0	0	0.0
7	13	1	0	7.7
8	4	0	0	0.0
9	5	0	0	0.0
10+	19	1	2	15.8
Control	46	2	0	4.3

Fig. 2.—Acute salpingitis.

Perivascular Round-Cell Infiltration.—The gathering of lymphocytes and plasma cells around the veins of the tubal muscularis is shown in Fig. 4. This cuffing of the veins occurs both in the pregnant and nonpregnant tubes with a fair degree of frequency. However, it would appear from Table III that this lesion is more prevalent during the pregnant state and the puerperium, espe-

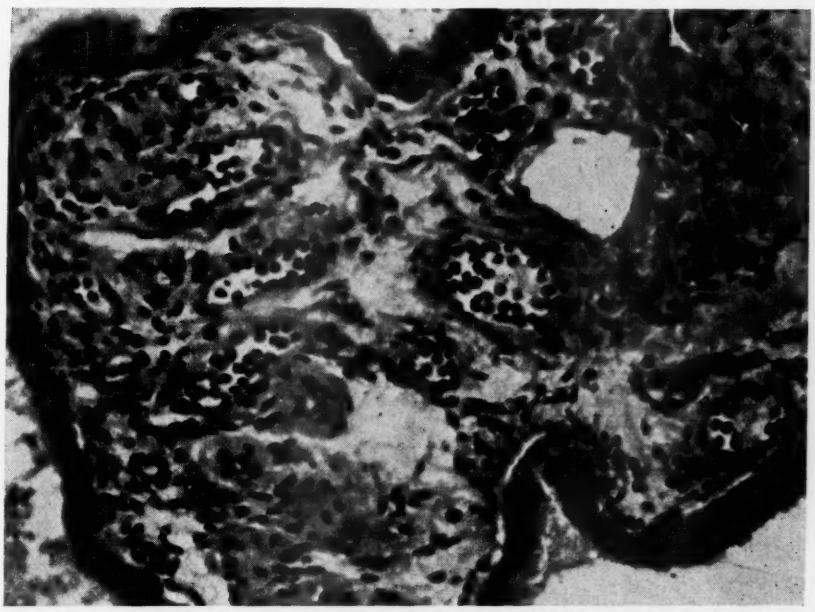

Fig. 3.—Leucostasis. Collections of polymorphonuclear leucocytes are seen in the veins of the tubal rugae.

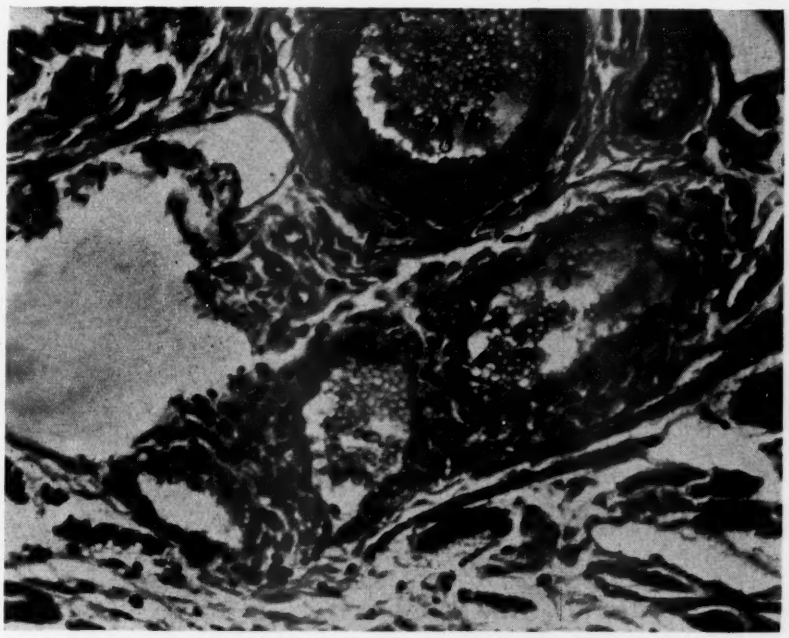

Fig. 4.—Perivascular round-cell infiltration. There is a cuffing of the lymphocytes around the veins of the muscularis.

cially from the third to the sixth puerperal days. This point of view is strengthened by the occurrence of perivascular round-cell infiltration in tubes of 35 per cent of the hysterotomies. This finding has no correlation with the presence or absence of syphilis in the mother, nor is it related to the occurrence of fever in the puerperium.

TABLE III. THE OCCURRENCE OF TUBAL PERIVASCULAR ROUND-CELL INFILTRATION IN 715 PUERPERAL STERILIZATIONS DISTRIBUTED ACCORDING TO TIME OF OPERATION

DAYS POST PARTUM	STERILIZATIONS	PERIVASCULAR ROUND CELLS ONE TUBE	PERIVASCULAR ROUND CELLS TWO TUBES	PER CENT PERIVASCULAR ROUND CELLS
0	165	14	17	18.8
1	178	6	9	8.4
2	158	6	12	11.4
3	90	9	13	24.4
4	48	6	8	29.2
5	24	0	5	20.8
6	11	2	0	18.1
7	13	0	1	7.7
8	4	0	0	0.0
9	5	0	2	40.0
10+	19	1	1	10.5
Control	46	1	4	10.8

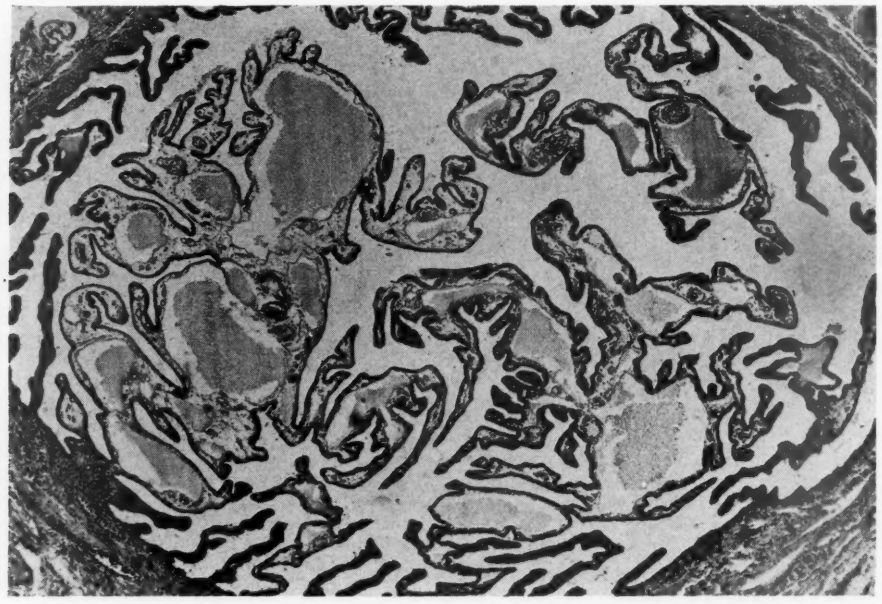

Fig. 5.—Tubal edema.

Tubal Edema.—Fig. 5 is typical of this lesion. The rugae are swollen and the lymphatic spaces greatly distended with acidophilic material. This does not extend to the muscularis. Table IV shows this form of edema to be related to pregnancy and the early puerperium. It was not found in this series after the seventh postpartum day and did not occur in the control group.

Decidual Reaction.—The presence of tubal decidua in relation to ectopic pregnancy and endometriosis has been reported by numerous observers. Tilden and Windstedt[4] have previously described its occurrence in association with

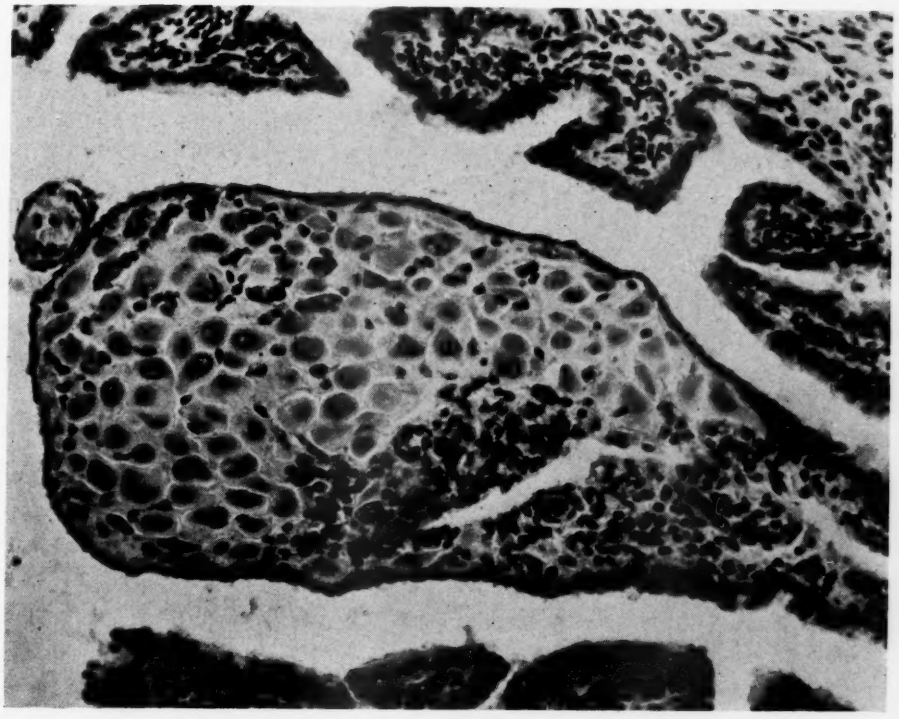

Fig. 6.—Decidual reaction.

Fig. 7.—Decidual reaction.

intrauterine pregnancy in 12 per cent of tubes removed within sixty-five hours of delivery. These authors thought that this high incidence had a racial relationship for it showed a much greater frequency in "the Hawaiian, or part Hawaiian," than in the Caucasian. The incidence in the present series is about half that of Tilden and Winstedt's for the same period of the puerperium. As one would expect, Table V shows that the presence of decidua is related to pregnancy and the early postpartum period. The decidual cells in all but one of the cases occurred in the stroma of the rugae. In no instance was the tubal epithelium involved, but it always appeared as a thin layer of cells covering the decidual bud (Fig. 6). Often, isolated tips of rugae with decidual change appear. These have a vague resemblance to immature placental villi and are often so called by inexperienced observers (Fig. 7).

TABLE IV. THE OCCURRENCE OF TUBAL EDEMA IN 715 PUERPERAL STERILIZATIONS DISTRIBUTED ACCORDING TO TIME OF OPERATION

DAYS POST PARTUM	STERILIZATIONS	EDEMA ONE TUBE	EDEMA TWO TUBES	PER CENT EDEMA
0	165	4	0	2.4
1	178	9	7	9.0
2	158	2	0	1.3
3	90	3	0	3.3
4	48	1	0	2.1
5	24	3	0	12.5
6	11	1	0	9.9
7	13	1	0	7.7
8	4	0	0	0.0
9	5	0	0	0.0
10+	19	0	0	0.0
Control	46	0	0	0.0

TABLE V. THE OCCURRENCE OF TUBAL DECIDUA IN 715 PUERPERAL STERILIZATIONS DISTRIBUTED ACCORDING TO TIME OF OPERATION

DAYS POST PARTUM	STERILIZATIONS	DECIDUA ONE TUBE	DECIDUA TWO TUBES	PER CENT DECIDUA
0	165	7	2	5.5
1	178	8	1	5.1
2	158	7	2	5.7
3	90	3	0	3.3
4	48	2	0	4.2
5	24	2	0	8.3
6	11	0	0	0.0
7	13	0	0	0.0
8	4	1	0	25.0
9	5	0	0	0.0
10+	19	0	0	0.0
Control	46	0	0	0.0

TABLE VI. THE OCCURRENCE OF RARE TUBAL FINDINGS IN 715 PUERPERAL STERILIZATIONS

PATHOLOGIC FINDING	NUMBER
Walthard cell rest	12
Cystic Walthard cell rest	4
Lymphangioma	1
Venous thrombosis	3
Endometriosis	1?

The rarer findings are listed in Table VI. Walthard cell rests, either solid or cystic, appeared sixteen times. These were often multiple and are quite typical of such rests found elsewhere, as in the ovary (Fig. 8). There was one

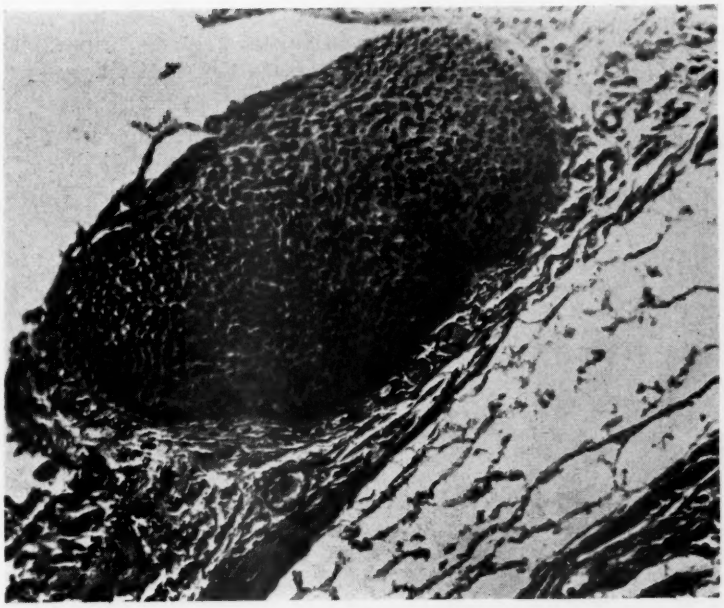

Fig. 8.—Walthard cell rest.

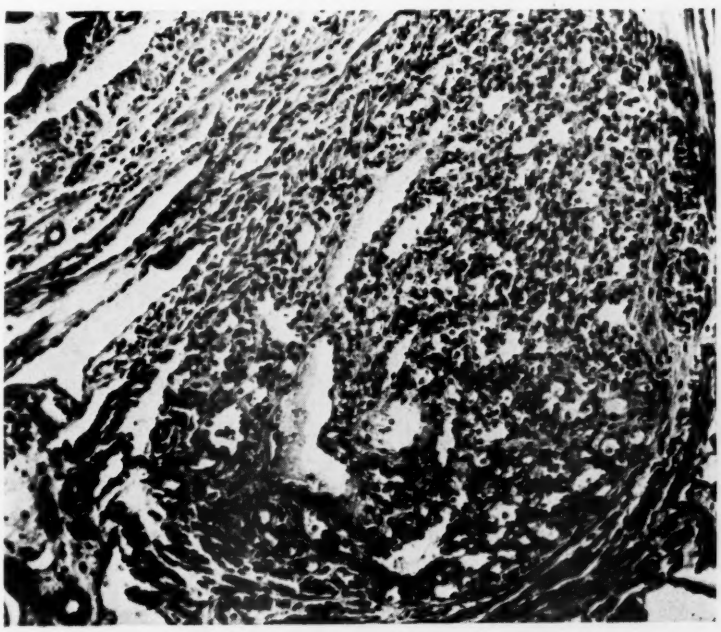

Fig. 9.—Lymphangioma.

lymphangioma, as illustrated in Fig. 9. These are small, well-demarcated tumors of the tubal muscularis. They are probably extremely rare because less than twenty have been reported in the literature.[5]

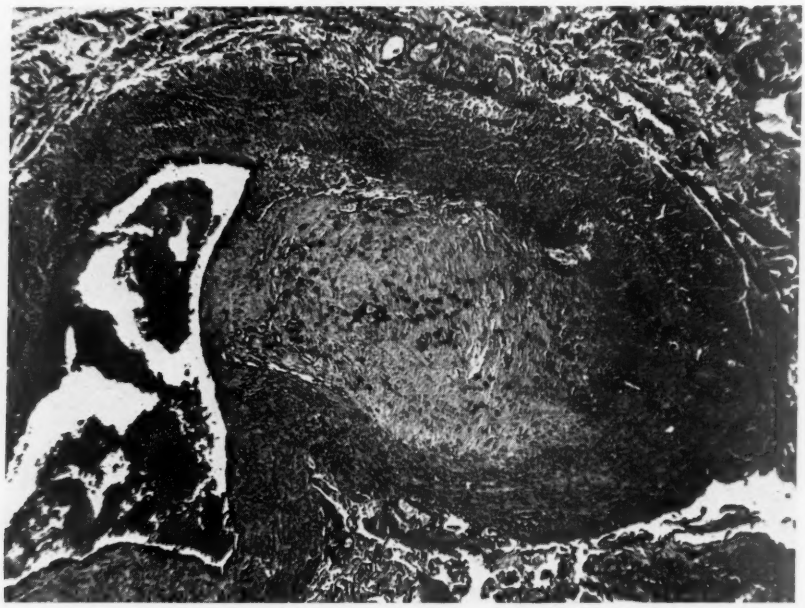

Fig. 10.—Venous thrombosis. This is a fairly old process as shown by the discoloration and partial organization of the thrombus

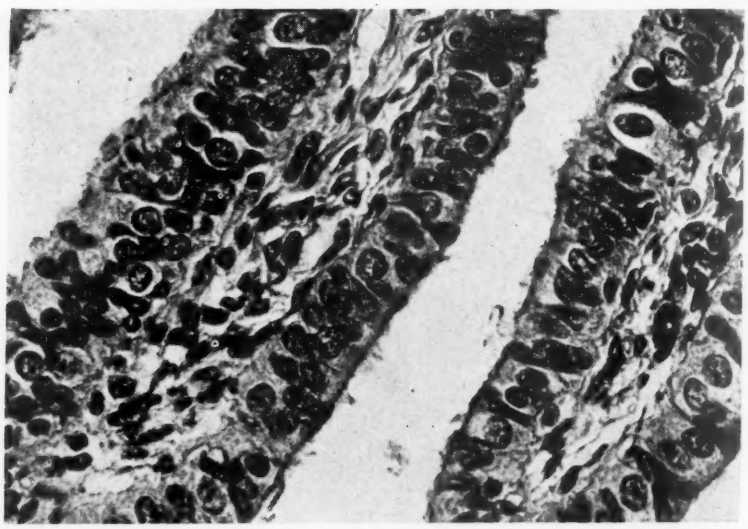

Fig. 11.—Postpartum mucosa. Note the rather high epithelium with evidence of secretion and extrusion of nuclei.

Venous thrombosis of the muscularis was present in three patients (Fig. 10). The thrombi were all similar and showed obvious discoloration and partial organization, all of which indicated that they antedated delivery by several days at least. Such thrombi must originate in varicosities of the mesosalpinx and may account for some of the unexplained emboli associated with labor and delivery.

The tubular epithelium was almost uniformly low at term, confirming the previous reports of Snyder,[6] Novak and Everett,[7] and Tietze.[8] The low epithelium rapidly increases in height and between the seventh and tenth postpartum day the epithelium is uniformly high. The "secretory" cells are level with the ciliated variety. Extrusion of nuclei is present (Fig. 11).

Conclusions

From a study of 715 pairs of Fallopian tubes, obtained at tubal sterilization on various days of the puerperium, the following conclusions are reached:

1. Acute salpingitis of nonspecific origin and in mild to moderate degree, occurs in one of every three puerpera, approximately between the sixth and eighth days, but is rare during the first four days.

2. Leucostasis may be observed in about 20 per cent of cases during the first twenty-four hours of the puerperium and in about 10 per cent during the second and third days, but is rare thereafter.

3. Perivascular round-cell infiltration, while present both in the pregnant and control groups, is definitely more frequent at term and in the first week of the puerperium.

4. Tubal edema is more prevalent at term and in the first week of the puerperium than at other times.

5. Decidual reaction has its most frequent incidence at term and in the early days of the puerperium, about 5 per cent of cases showing it at this time.

6. Scattered instances of Walthard cell rests, venous thrombosis, and one case of lymphangioma are reported.

7. There is a rapid change in the tubular epithelium from a low to a high secretory phase during the first week of the puerperium.

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Discussion

DR. HOUSTON S. EVERETT, Baltimore, Md.—Dr. Hellman's paper consists of the presentation of carefully observed facts, concerning which it may be presumed that there are no grounds for disagreement or controversy. He has made little or no effort to interpret the significance of these observations. From the discusser's point of view, therefore, the only opportunity presented is to attempt to postulate interpretations of some of the more interesting of the observed facts, and perhaps to suggest further lines of investigation designed to throw more light upon such postulated interpretation.

To me, the most interesting of the observations is the high incidence of acute salpingitis in those segments of tubes removed during the later days of the puerperium. Some of the individual day groups are too small to be of percentage significance. If, however, we condense Dr. Hellman's Table I, we find that, of 539 cases in which the tubes were removed during days 0 to 4 inclusive, only 13, or 2.4 per cent, showed acute salpingitis. In contrast, of the group subjected to operation during days 5 to 10 inclusive, acute salpingitis was found in

the tubal segments from 17, or 22.4 per cent of the 76 cases. This finding would suggest that patients sterilized early in the puerperium would be less apt to show morbidity during their poststerilization convalescence than those operated upon during the later days of the puerperium. Indeed, Dr. Hellman has told me that this was true in his series of cases, but that he was not able to determine that these patients whose tubes showed acute salpingitis were the particular ones who exhibited postoperative morbidity. Whitacre, on the basis of clinical observation, plus the fact that of 100 intrauterine cultures taken during the puerperium only 13 were sterile, and that these 13 were all taken during the first few hours following delivery, has concluded that if postpartum sterilization is to be done, it should always be done in the first few hours following delivery.

Whitacre's bacteriologic findings would suggest that the observed salpingitis is probably of infectious origin. It seems to me, however, that it might very well be a noninfectious inflammation extending from the uterine cavity where the necrosis and sloughing of the decidual remnants are always associated with leucocytic infiltration. It is suggested that in a future study small fragments of the tubal segments that are to be subjected to microscopic study also be subjected to bacteriologic culture. It could thus be determined whether or not those tubes which show acute salpingitis have actually been invaded by bacteria.

Finally, the morphology of the tubal epithelium as found by Dr. Hellman in those segments of tubes removed at cesarean section or immediately after delivery coincides with that described by Dr. Novak and myself, in 1928, as typical of the pregnant state. The epithelium presented as typical of that from tubes removed from the seventh to the tenth days post partum corresponds most closely with that found by Dr. Novak and myself in tubes removed at the midinterval of the menstrual cycle. Since most patients do not menstruate for six weeks or more following delivery, one wonders what happens to the tubal epithelium in advancing from this phase to the ones which we recognized as characteristic of the premenstrual and menstrual phases of the cycles. In the regularly menstruating woman, these changes ordinarily occur over a period of approximately two weeks.

DR. CARL HUBER, Indianapolis, Ind.—The present study represents a diligent investigation of the morphology of a large number of tubal specimens obtained during the immediate puerperium. All of these specimens are presumed to be of normal tubes as they were functionally capable of permitting pregnancy and were removed from postpartum patients who showed no febrile morbidity. They should, therefore, be indicative of the changes produced in the tube by pregnancy and delivery. Unfortunately, they do not demonstrate any consistent variation from the normal tube in the nonpregnant woman.

These observations would suggest: 1. The endocrine changes in pregnancy do not have an important effect on the appearance of the tube. 2. The mechanical changes produced during pregnancy and delivery do not have any consistent effect on the microscopic structure. This would be anticipated as the tube following completion of the puerperium is normally unchanged both microscopically and functionally.

Of the variety of structural variations described, only the appearance of decidual reaction in the tubal mucosa would seem to be entirely characteristic of pregnancy. This appears in only a small percentage of the tubes examined and, as is well recognized, is not the only extrauterine site where it may be found.

The other conditions which may logically be related to pregnancy and the puerperium are edema, leucostasis, and perivascular round-cell infiltration. They seem to be of doubtful significance and far from constant. They may well be related to the regressive changes which are occurring in adjacent structures and to mechanical variations in the vascular supply of the pelvic organs, as the result of termination of the pregnancy.

It is suggested from the report that bacterial invasion of the tubes is not a frequent finding following normal delivery, in comparison to the bacterial invasion of the uterine cavity which quite normally does occur.

I believe that we are indebted to the author for his description of the morphology of the puerperal tube. There has previously been a gap in our exact information concerning this phase.

DR. HELLMAN (Closing).—In reply to Dr. Everett, I would say that we were disappointed that we could find no correlation between the microscopic finding of an acute salpingitis and an acute febrile postoperative course. However, the later one waits to perform this operation, the more likely one is to find a febrile course.

In regard to the high epithelium that Dr. Everett mentioned, we are now carrying on further studies. We are actually measuring the height of the tubal epithelium at various days of the puerperium, to see whether this rapid growth is connected with lactation. Also, the oxygen requirement of the tubal mucosa changes with the menstrual cycle, and studies are being carried out on the metabolism of tubes at various stages of the puerperium.

Dr. Huber has reviewed our findings excellently. It is true that leucostasis is found to some extent in normal tubes. However, there is a greater frequency in pregnancy and therefore that was stressed in this paper.

OVARIAN PREGNANCY*

With a Report of Three Cases

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(From the Department of Obstetrics and Gynecology, University of Rochester)

OVARIAN pregnancy is one of the rarest forms of extrauterine pregnancy, only primary abdominal pregnancy being encountered less frequently. According to Williams,[4] ovarian pregnancy was first described in the seventeenth century by Mercerus and St. Meurice. It was regarded as a real, though rare, possibility until Velpeau in 1835 expressed skepticism concerning many of the previously described specimens and doubted if it could occur at all within the substance of the ovary. While most German authors have admitted its possible occurrence, English and American authors in general denied its possibility until 1899, when Tussenbroek[3] gave an accurate description of one, to be followed three years later by the report of the first one described in this country, by Thompson[2] in 1902. Today, any discussion as to the possibility of its occurrence is of only academic interest, and numerous examples of undoubted authenticity have been presented in the literature.

It is of importance, of course, that certain criteria be observed in deciding whether a particular case actually does represent a true ovarian pregnancy. Those criteria formulated by Spiegelberg[1] in 1878 are the ones which are accepted as being the "sine qua non" before a particular pregnancy may be regarded as a true ovarian pregnancy.

In regard to the mode of origin of an ovarian pregnancy, some facts are known, while other factors involved offer an interesting field for speculation and are as yet unsolved. When we recall that complete maturation of the ovum is necessary before fertilization can occur, it becomes obvious that, for a pregnancy to take place in the ovary, there must be a variation from the usual course of events. While the first polar body may be extruded from the ovum while still within the ovary, the second polar body is ordinarily not cast off until the ovum is expelled from the follicle. If on occasion, however, maturation of the ovum is completed while the ovum is still in the follicle with the latter ruptured, a sperm cell could enter, fertilize the ovum, and the pregnancy begin in situ. Robert Meyer, on the other hand, believed that most often a cortical implantation of the ovum occurs with later invasion of the ovarian stroma. Novak states that, after its discharge, the ovum may be fertilized and then be implanted in the follicle or corpus luteum (intrafollicular implantation), the trophoblast soon penetrating these and invading the deeper structures (juxtafollicular implantation). Probably any of these mechanisms may occur, but only if one had

*Read at the seventy-first annual meeting of the American Gynecological Society, Williamsburg, Virginia, May 24 to 26, 1948.

the extremely good fortune to encounter an ovarian pregnancy in the very early stages, could one provide an accurate answer to these questions.

The symptoms and findings on examination are those common to ruptured tubal pregnancy and may be slight, making diagnosis difficult, or may be severe with profuse intra-abdominal hemorrhage. Rupture may be early but, generally speaking, it is likely to occur rather later than is the case in tubal pregnancy. A positive diagnosis cannot be made until the abdomen is opened and the involved structures removed for study.

Fig. 1.—A cross section of the whole ovary from Case 1, under low magnification (×6.5). Note the large clot containing the pregnancy and the adjacent corpus luteum—juxtafollicular implantation.

In spite of its rarity, we have had the opportunity of observing three examples of ovarian pregnancy, all of which satisfactorily fulfill the criteria as laid down by Spiegelberg. These three cases occurred in a series of 224 of the various types of extrauterine pregnancy.

CASE 1.—V. S., unit No. 104482, aged 29 years, para ii, was admitted to Strong Memorial Hospital on July 8, 1935. Her past history is irrelevant except for two normal, full-term pregnancies and two miscarriages. The last menstrual period began May 22, 1935, and was normal. On June 22, 1935, daily "spotting" began and continued until July 3, when a more active flow began, accompanied by crampy lower abdominal pain. The day after admission, she expelled some tissue which on examination was found to be decidua. Her symptoms subsided and she was discharged. No demonstrable mass was noted on pelvic examination at the time of discharge and she was regarded as a complete abortion. She was readmitted two weeks later, on August 1, 1935, with recurrence of right-sided lower abdominal

Fig. 2.—Early chorionic villi, detached and lying in the clot noted in Fig. 1. (×100)

pain but no bleeding. Her general condition was good: temperature 38° C.; pulse 90; blood pressure 115/72. The red blood cells 4,100,000, hemoglobin 11 Gm., and white blood cells, 9,000. Abdominal examination revealed some tenderness and slight spasm in the right lower quadrant, while on pelvic examination, a sensitive, semicystic mass about 6 cm. in diameter was found to the right of the uterus. A diagnosis of ectopic pregnancy was made and operation carried out. On opening the abdomen, no free blood was encountered. The right appendages were somewhat adherent and included a small mass of attached blood clot. The right tube and ovary were removed; also the appendix. Her convalescence was uneventful.

Description of Specimen.—The right tube was grossly normal. The right ovary measured 5 by 5 by 4 cm. and was partially covered by adherent blood clot. On bisecting the ovary, a well-developed corpus luteum was observed in one pole of the ovary, while adjacent

to this is a mass of old blood clot which appears to be surrounded by a thin, membranous structure. This mass measured 2 by 2½ cm. in diameter. What grossly appears to be ovarian tissue surrounds both the corpus luteum and the small mass of clot. On microscopic study, the well-formed corpus luteum is observed, though the cells are undergoing degenerative change. Adjacent to this, but definitely separated from it, is the mass of clot, embedded in the substance of the ovary and in which a number of early chorionic villi are seen. Most of them lie loose in the clot, but an occasional villus is found attached to the margins of the sac, fastening villi. No trace of an embryo was found. A layer of undamaged ovarian tissue is demonstrable throughout the specimen except at one point which probably represents the site of rupture. No decidual reaction is noted. Numerous sections through the tube showed it to be anatomically intact, but did show some degree of chronic inflammatory reaction. (Figs. 1, 2, 3.)

Fig. 3.—Two fastening villi attached to the wall of the sac, which is ovarian tissue. (Case 1.) (× 100)

It is interesting to speculate, but one can only speculate, on the mode of implantation here: The fact that the corpus luteum is undamaged by any invasion of trophoblast, while the site of the pregnancy lies beneath this, probably means a rapid invasion of the stroma of the ovary after fertilization had occurred, with no interference to the development of the corpus luteum—juxtafollicular implantation.

Case 2.—M. A., unit No. 161938, aged 30 years, was admitted to Strong Memorial Hospital on Feb. 4, 1940, under the care of Dr. C. A. Elden. Her past history is irrelevant except for the occurrence of two normal, full-term pregnancies What she described as a normal

menstrual period occurred from January 27 to February 3, her previous menstrual period having occurred on December 25. She began to have intermittent episodes of rather severe left lower quadrant pain on January 18 and these continued at intervals until admission.

On admission, temperature was 37° C., pulse 98, blood pressure 109/78. The red blood cells, 4,100,000, hemoglobin 13 Gm., and white blood cells 13,000. Abdominal examination showed marked tenderness and spasm in the left lower quadrant. Pelvic examination revealed an exquisitely sensitive cystic mass at the left of the uterus whose dimensions could not be easily outlined on account of the marked tenderness. A diagnosis of ruptured ectopic pregnancy was made and operation carried out by Dr. C. A. Elden.

On opening the abdomen, considerable dark blood was encountered. The sigmoid, omentum, and small bowel were adhered to the left appendages. After freeing them, the left tube and ovary were removed; also the appendix. The convalescence was uneventful. This case presents an unusually early rupture of an ovarian pregnancy.

Fig. 4.—A low-power (×7.5) magnification of a segment of the ovary in Case 2. Note the clot adjacent to the corpus luteum and compressing it on one side. Another example of juxtafollicular implantation.

Description of Specimen.—The left tube was somewhat enlarged but intact. The ovary was a cystic structure 6 cm. in diameter with a small jagged rupture, 1.5 cm. in diameter, in its posterior aspect. On opening the specimen further, a well-developed corpus luteum was found and adjacent to this, and embedded in the ovarian stroma, was a larger mass of clot 4 cm. in diameter.

On microscopic examination, the findings were quite comparable to those described in Case 1. The corpus luteum was intact, but was markedly compressed in its lower side at the point adjacent to the blood clot, from which it was separated by a thin layer of connective tissue. The lutein cells were undergoing degenerative changes. At this point, too, a few trophoblastic cells were seen intermingling with the lutein cells but there had been no active destruction of lutein cells by the few invading fetal cells. Embedded in the clot were numerous well-formed early chorionic villi. Ovarian tissue was demonstrable, covering the remainder of the clot except at the point of rupture. No decidual reaction was noted. No trace of an

embryo was seen. Numerous sections of the tube showed it to be intact but a chronic inflammatory reaction was found. The mechanism of implantation and development in this pregnancy were probably identical with those occurring in Case 1. (Figs. 4, 5.)

CASE 3.—M. F., unit No. 190991, aged 34 years, was admitted to Strong Memorial Hospital on April 9, 1947. Her past history is irrelevant except for the occurrence of two normal, full-term pregnancies, five and two years previously. Her last menstrual period occurred on March 14, 1947. The night before admission, she had an episode of acute lower abdominal pain with onset of slight vaginal bleeding. On admission, she was in a state of mild shock. Blood pressure 100/60, temperature 37° C., pulse 54, and white blood cells 6,000.

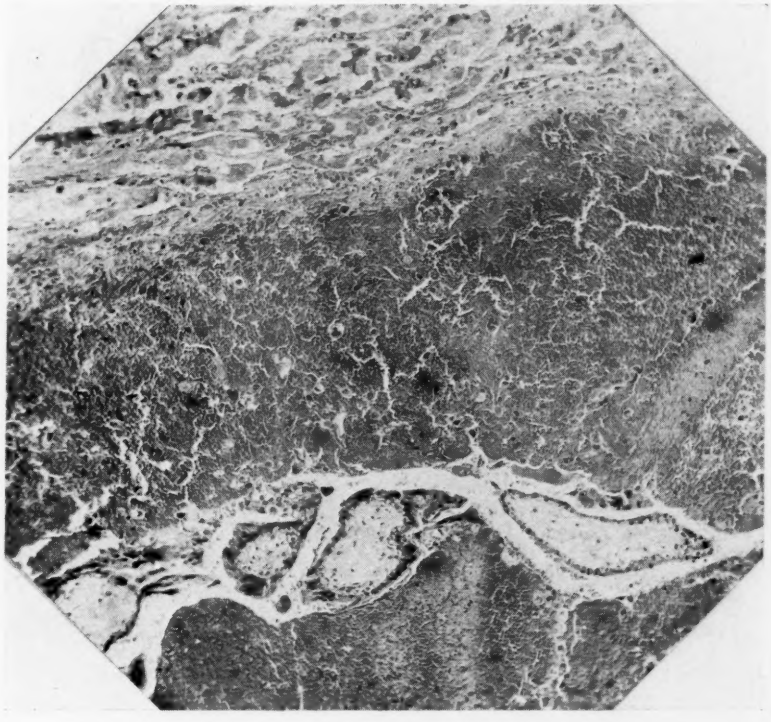

Fig. 5.—Early chorionic villi embedded in the clot adjacent to the corpus luteum in Case 2. (× 100).

Examination revealed an acutely inflamed abdomen, with signs of internal hemorrhage. On pelvic examination, a cystic bulging mass was felt in the posterior cul-de-sac. A diagnosis of acute ruptured ectopic pregnancy was made and immediate operation carried out, a transfusion of 1000 c.c. of whole blood being begun at the same time. When the abdomen was opened, a large amount of old and fresh blood was encountered, at least 1000 c.c. The right appendages were found to be normal as was the left tube, but the left ovary was somewhat enlarged and, on its outer aspect, presented a dark cystic area about 1.5 by 2 cm. in diameter. In the lateral region of this was a small rupture through which free bleeding was occurring. The left tube and ovary were removed. Her convalescence was uneventful.

Description of Specimen.—The tube was intact and grossly appeared quite normal. The ovary measured 4 by 2.5 by 2 cm. On one side was a rent through which a fragment of blood clot protruded. When the ovary was bisected, a clot 2.5 by 1.5 cm. was found immediately under the surface; also a small follicular cyst adjacent to this. The ovarian stroma was

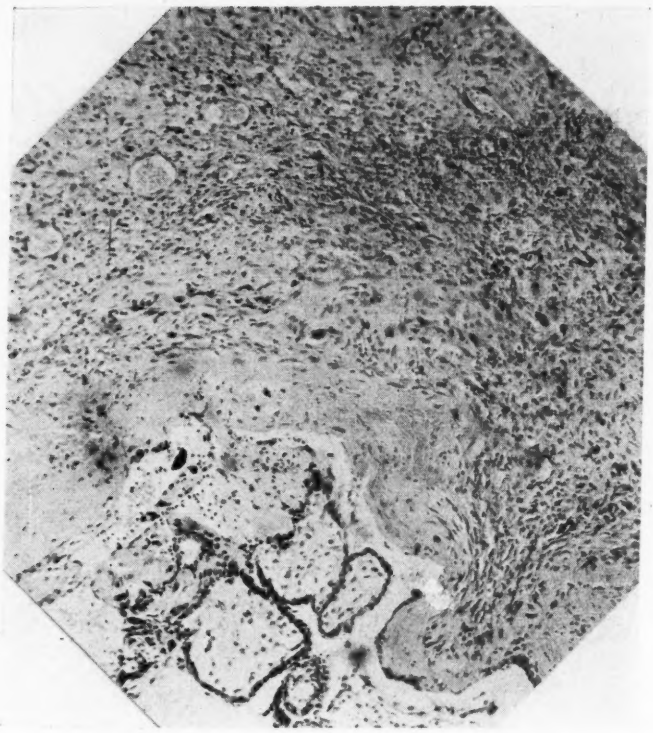

Fig. 6.—Early chorionic villi embedded in the substance of the ovary in Case 3. Note also the rather active invasion of ovarian stroma by trophoblastic cells. (×100)

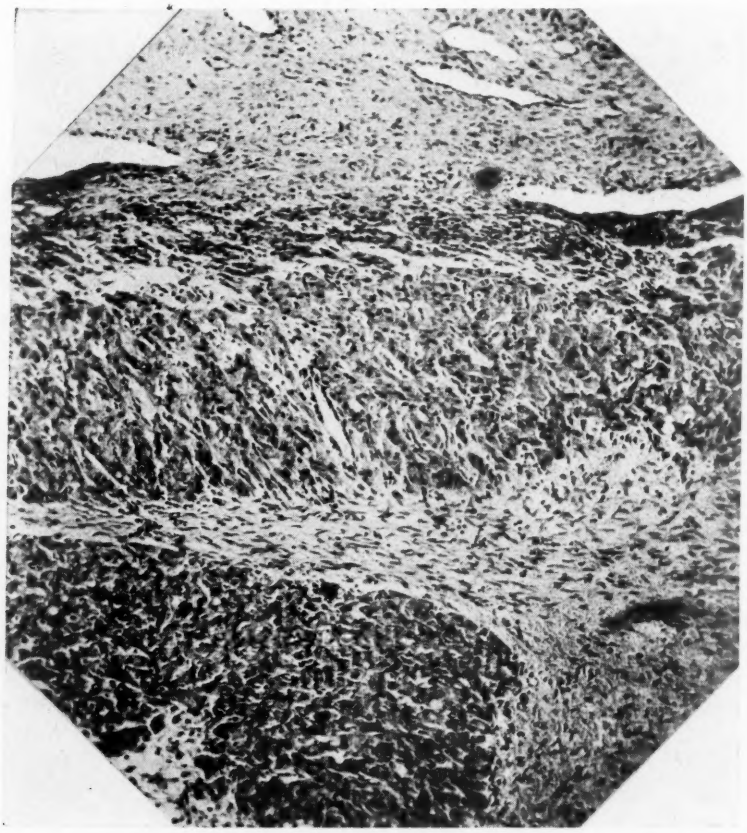

Fig. 7.—A portion of the corpus luteum near the pregnancy but not in such close proximity as in the other two cases. (× 100)

greatly thinned out around the clot and a small corpus luteum was observed. A small membranous sac measuring 4 mm. in diameter was found embedded in the blood clot and may have represented fetal membrane, but no gross embryo was seen. On microscopic study, a fragment of the chorionic membrane to which early villi were attached was found embedded in the clot, also numerous other normal-appearing early villi which had been broken off from their attachments.

Adjacent to part of the clot, but in the ovarian stroma, was an irregular fibrinous layer, suggestive of Nittabuch's fibrin layer as seen in uterine implantation. There was also some invasion of the ovarian stroma by trophoblastic cells. The corpus luteum was well developed but was broken on one side, apparently the result of trauma incidental to the rupture of the sac. Nothing suggesting a decidual reaction was noted in any of the slides studied. (Figs. 6, 7.)

Summary

Three examples of ovarian pregnancy are presented, each of which fulfills the criteria necessary for making such a diagnosis. From the clinical standpoint, one of them presented a diagnostic problem, while the other two presented findings which readily permitted a diagnosis of ectopic pregnancy, and one was an extremely acute case, with extensive intraperitoneal hemorrhage. Cases 2 and 3 represent an unusually early rupture. Study of the specimens revealed in two of them well-developed corpora lutea adjacent to the pregnancy, the so-called juxtafollicular implantation, but whether this was preceded by fertilization in the actual follicle or on the surface of the ovary, it is, of course, impossible to say at the present time. The well-developed and intact corpora lutea so close to the pregnancy rather suggest fertilization in the follicle, followed by rapid invasion of the underlying ovarian stroma. In none of the specimens was any decidual reaction noted.

The fate of the ovum in ovarian pregnancy is comparable to that which takes place in other forms of extrauterine pregnancy; namely, development for a period of time, with associated erosion of the adjacent tissues and eventual rupture, with sometimes slight and sometimes severe symptoms. While we have not encountered an example, it is interesting to note that a higher percentage of ovarian pregnancies proceed to term than is the case with tubal pregnancy, this being no doubt due to the more resistant type of tissue in which the pregnancy is embedded.

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Discussion

DR. JOHN ROCK, Brookline, Mass.—Dr. Wilson calls our attention to an intriguing disturbance of reproductive physiology. Symptomatology, diagnosis, and treatment, as Dr. Wilson says, are those of ectopic gestation in general.

To the biologist it may seem possible that an entrapped ovum cleaves and develops parthenogenetically. Autogenous ovular growth is found in several forms that are, at least schematically, lower among animals than we are. Clinical histories are so heartlessly intrusive and so shamelessly published, they would surely have adorned Christian medical literature with more than one case of virginal gestation if parthenogenesis could explain ovarian pregnancy.

It has been suggested that speedy and adventuresome spermatozoa may leave the tube and rush through the follicular breach successfully to attack the lingering ovum. This postulate would be difficult to substantiate.

The second, or reduction division of chromosomes that Dr. Wilson has mentioned, usually takes place some time after the first phase of myosis, that produced the first polar body just before follicular rupture. This first myotic division results from only a longitudinal split, not the necessary numerical halving of the chromosomes which occurs probably in several hours. When the follicle ruptures, as it must if spermatozoa are to enter, fluid is released, pressure diminished, the granulosa is partly disrupted and, inevitably, hemorrhage into the antrum occurs before myosis could be completed. Now the enzyme, hyaluronidase, produced by spermatozoa, must be at least an adjunctive agent for dispersal of the corona radiata, for there is hyaluronic acid among the granulosa cells investing the egg. An antihyaluronidase factor has been found in the blood serum of various species. Other enzymes may be essential to the penetration of the vitelline membrane and, for them, too, there may be in the blood inactivating factors. At all events, fertilization in vitro of rabbit and human eggs has not been achieved in the presence of blood, and preliminary experiments by Finkle at the Free Hospital for Women tend to show that if there is blood in the rabbit tube fertilization in vivo fails. I think this would likewise be the case within the human follicle.

Meyer's and Novak's explanation of ovarian pregnancy is easy to accept. Sperm do not live long in peritoneal fluid. It seems likely that the eventually ectopic ovum finds temporary shelter and spermatic service within, at least, the protective fimbriae of the tube. After activation by the sperm, a failure of tubal peristalsis (for the ciliary current must be a weak force as applied to the bulky ovum) leaves the zygote where it is or reverse peristalsis ejects it.

Dr. Wilson notes that no decidua was found in his specimens. By several workers, Runner, Fawcett, Wislocki, Waldo, and Nicholas, transplantation to the eye, the kidney, even onto the peritoneum of mouse eggs fertilized in vivo has shown that access to nothing more than circulating blood will permit trophoblastic growth. Study of normally implanted conceptuses leads one to suspect that the trophoblast seeks, not primarily decidua, but maternal blood. In the late secretory endometrium, the substantial stroma gives support to the vascular sinusoids, the endothelial cells of which readily submit here and there to engrossment by the syncytium.

I believe it likely that so long as the integrity of invaded maternal vessels and adaptive sinuses containing good blood is maintained by surrounding tissues and the site of entry plugged by the trophoblast, conceptual growth continues. When available blood is deficient or becomes insufficient for the rapidly growing normal "neoplasm," or the local inadequately buttressed maternal vascular system ruptures, abortion occurs. The reason, perhaps, why, as Dr. Wilson points out, an ovarian pregnancy progresses further than the tubal variety is because of the greater expansion-potential of the more elaborate and more firmly supported blood supply of the ovary, beneath the cortex of which the phagocytic syncitiotrophoblast succeeded in imbedding the conceptus.

DR. JOHN I. BREWER, Chicago, Ill.—The three specimens are of extreme interest because the ovaries containing the pregnancies were only slightly enlarged. The relationship of the ovarian structures and the implantation sites can therefore be determined. The embryonic mass is not within the corpus luteum and there is not the least suggestion that it had been previously. Those trophoblastic elements that are intermingled with corpus luteum tissue are obviously invading the corpus luteum from without. In larger and older specimens in which the relationships are more disturbed, it is impossible to draw conclusions. Confusion in interpretation also may result from failure to differentiate decidual tissue in the ovary from corpus luteum tissue.

It is logical to assume that implantation phenomena are fundamentally similar in an ovarian pregnancy and in a pregnancy in the endometrium. Implantation is on the surface. The embryonic mass enters the maternal tissue and becomes buried. No evidence of surface

implantation remains. The sequence of events explains the findings in the described ovarian pregnancy more reasonably than does the supposition of intrafollicular implantation for which there is no evidence and no proof.

Another interesting point for discussion is contained in the history of the first patient. The patient was discharged from the hospital after she had passed some tissue from the uterus which on examination was decidua without chorionic tissue. The symptoms had also subsided. The diagnosis was a complete abortion. Subsequently the extrauterine pregnancy was proved.

The finding of decidual changes in the endometrium without chorionic tissue suggests an extrauterine pregnancy. All efforts should then be made to make such a diagnosis. There are exceptions to this rule, of course. (1) Chorionic tissue may be missed because the entire specimen is not available for examination. (2) The few microscopic sections that are usually made of a given specimen may not include the chorionic tissue. (3) The entire trophoblast may have been aborted prior to the time the specimen is obtained for examination. (4) Decidua may be present without pregnancy. TeLinde described several such instances. One patient of ours had metrorrhagia and menorrhagia of six years' duration. A dilatation and curettage was done for diagnosis. The endometrium was proliferative in type and there was no chorionic tissue. Ten weeks later, after a continuation of the abnormal bleeding, the uterus and the corpus luteum were removed abdominally. The endometrium had a well-differentiated decidual reaction. The corpus luteum was regressing. Complete study of the uterus and gross inspection of the tubes and ovaries revealed no pregnancy. Decidual changes in the endometrium have been described in patients with certain ovarian tumors in the absence of pregnancy. Decidual tissue has also been produced experimentally in the human endometrium by prolonging the life of the corpus luteum with chorionic gonadotropin. While it is true that decidua may be present without pregnancy, it is our belief that such is relatively rare. (5) It is possible for an extrauterine pregnancy to resolve spontaneously in rare instances. In such a case, decidua may be obtained from the uterus with no chorionic tissue. The patient gets well and a pregnancy is not proved. With these things in mind, however, the rule still holds that decidual changes in the endometrium in the absence of chorionic tissue strongly suggest the presence of an extrauterine pregnancy.

Absence of decidual reaction in the endometrium does not mean that the patient is not pregnant. Early in a normal uterine pregnancy, decidua may not be present, as Hertig and Rock and we have observed. Early in an extrauterine pregnancy, and in those patients in whom symptoms have been present for some time, there frequently is no decidual tissue in the endometrium.

DR. WILSON (Closing).—Dr. Rock emphasized much more strongly than I did the very complicated process of the implantation of the ovum in the ovary. From the specimens shown, one can only speculate in regard to the mechanism of this. What would be needed to get actual information would be for someone to find a very early ovarian pregnancy that had not yet ruptured. I am not aware of such a one having been reported.

I think the decidual reaction is not important. Of course, if there be any endometrium in the ovary one will get decidua developing in this tissue.

OBSERVATIONS ON THE ROOMING-IN PROGRAM OF BABY WITH MOTHER IN WARD AND PRIVATE SERVICE*

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ON JULY 12, 1947, the policy of rooming the normal, full-term, newborn baby with its mother was inaugurated in the obstetric wards of the Jefferson Medical College Hospital. From that time until April 12, 1948, which represents the period covered by this study, 1,018 newborn babies were cared for in this fashion. Of these, 926 were the offspring of ward patients; 92 were the babies of private patients who were cared for in a low-cost, semiprivate ward. While the obstetric wards, which were built some twenty years ago, were originally planned with no thought of such a project, yet actually the architectural arrangement lent itself quite well to this undertaking and it was found unnecessary to make any physical alterations.

The ward service consists of six rooms, each containing six beds. Each of the wards has its own bathroom, each has its own wash basin quite accessible within the ward space (Fig. 1). The rooms are ordinarily well heated, and the windows are protected by ventilators. In addition to the six wards for obstetrical patients, there is a labor room of four beds, a nursery for full-term babies, a premature nursery, an isolation nursery, a formula room, a central office, a sterilizing room, service rooms, etc. All of these occupy one floor of the Samuel Gustine Thompson Annex, the wards and nurseries being arranged in a rectangular fashion about a central office. There is free visibility from the corridors into the rooms and from one ward to another by glass windows. The nurses, residents, internes, student clerks, etc., circulate rather constantly through the various parts of the floor so that mothers and babies are under frequent observation during the day, and not infrequent observation at night.

Procedure

Babies are kept in cribs at the mother's bedside both day and night unless one or the other is ill, or unless at night an individual baby is unusually noisy.

At first, the equipment for the care of the mother's breasts and of the baby was placed on a central table in each ward but it was soon observed that this arrangement would permit of cross-infection, and was also inconvenient to mother and nurse. In order to overcome this difficulty, a small crib-wardrobe was designed which the hospital carpenter constructed and which is hung on the end of each baby's crib. The crib-wardrobe consists simply of an upper and lower shelf. The top shelf contains covered jars for alcohol sponges, water sponges, dry cotton balls, and used sponges. The larger lower shelf contains the supply of individual diapers, pads, and blankets for a day's usage (Fig. 2).

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With this arrangement, the mother can readily reach her baby and the materials for its care while she is lying in bed or sitting on the edge of the bed; and no one touches these materials except herself (Fig. 3). The wardrobe can be readily lifted from the end of the crib and is constructed without covers or drawers so that it is easily and thoroughly washed with soap and water. This arrangement has worked most successfully, at an expenditure of not more than five or six dollars per crib, and has made it possible for us to provide quite efficiently for the individual care of each baby.

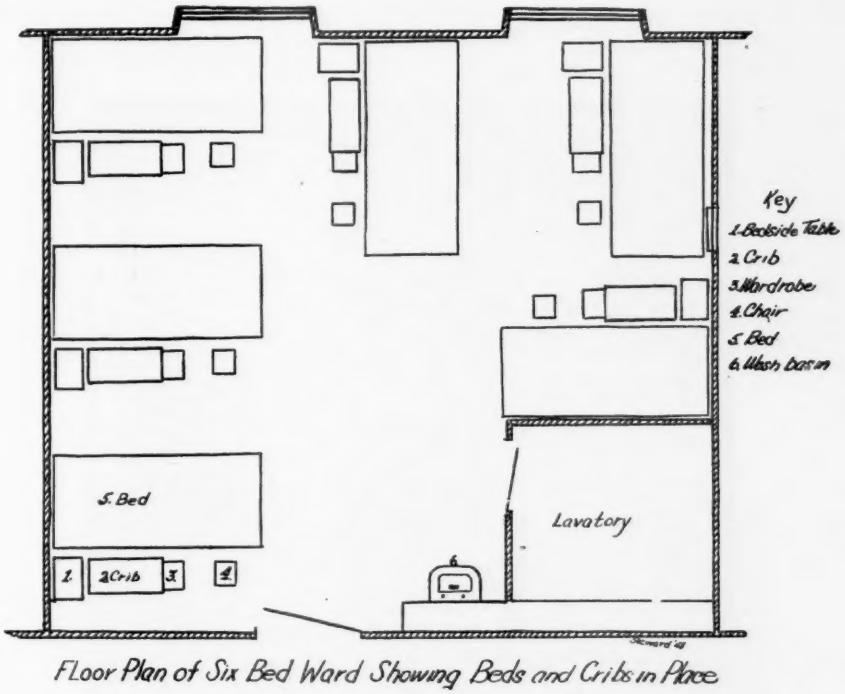

Fig. 1.—General plan of a 6-bed ward room.

Healthy, normal, full-term babies are placed with their mothers very soon after delivery. If the baby has considerable mucus in its pharynx, it is kept in the central nursery until this has cleared and respiration is normal. If the delivery is during the night, the baby may not be placed with the mother until the next morning. In not a few instances, however, the baby is at the mother's bedside within two to three hours after delivery. The practice is for the attendant in the delivery room to call the ward nursery when a delivery is completed and the newborn baby's condition determined to be satisfactory by the attending obstetrician. An individual stand, crib, and wardrobe is then prepared and the baby transported by the nursery attendants to its freshly prepared habitation in the nursery. Within a short time, with the exceptions mentioned above, the baby is beside the mother in the ward. Baby and mother are generally ready for this intimate association at an early hour for we employ little sedation during labor, light inhalation anesthesia for delivery, and local anesthesia for episiotomy and repair.

During the first twenty-four hours after delivery, the nurses take a great deal of time with these patients, demonstrating the technique of nursing and of

baby care, and emphasizing constantly the importance of cleanliness. The mother is encouraged to move freely in bed and participate in these various activities, but ordinarily she does comparatively little for her baby during the first twenty-four hours other than observe its progress.

By the end of twenty-four hours, the mother is generally out of bed, and thereafter conducts practically all of the routine care of herself and of her baby. She goes to the lavatory, uses the central wash basin, and sits either on the bedside or on a chair by her baby's crib. She calls upon the nurse in case of question or difficulty, but she learns very quickly to manage all ordinary situations and ordinarily gives her offspring excellent attention. From that time on until discharge, the nurses have very little to do with respect to feeding or changing of the baby.

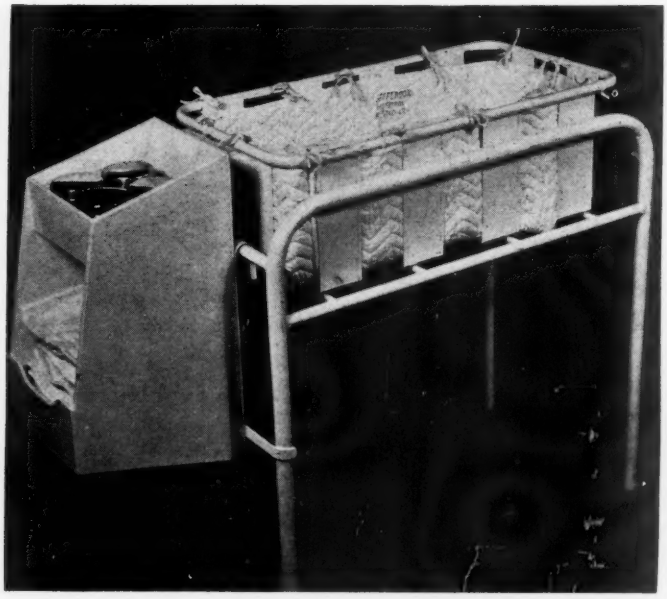

Fig. 2.—Crib wardrobe equipped and attached to crib.

Each morning the mothers are supplied with an individual "bath pack" containing a fresh change of clothing for the baby, fresh materials for the crib, baby blanket, and a sterile sheet of paper for weighing on the scales. Ward rounds are then made by the nurses from the central nursery employing a ward carriage equipped with scales, antiseptics, dressings for the navel, thermometers, and emergency drugs (Fig. 4). As this equipage comes along, the mother undresses her baby on her bed, changes the linen in the crib, puts the sterile sheet of paper on the scales, and watches her baby being weighed. She also watches the cord dressing changed and is instructed in the cleansing of neck, axilla, groin, vulva, with sterile swab and sterile water. Most mothers, even multiparas, are surprised and rather concerned at the presence of the stump of umbilical cord, never having noted it before in the course of baby care. Upon the occasion of these morning rounds, the nurses make their records of the baby's weight and temperature, and obtain from the mother's record of the previous twenty-four hours the data concerning nursing periods and baby's bowel movements. Twice in the course of her eight hour duty, the graduate in charge of the nursery makes rounds and personally checks on all babies. In the meantime, the babies are under almost constant observation of the floor nurses.

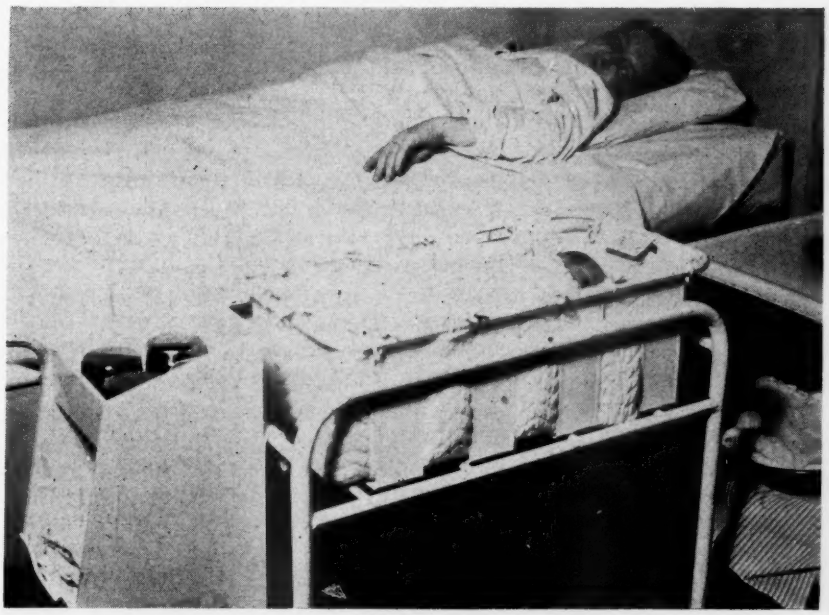

Fig. 3.—Baby and equipment at bedside of mother.

Fig. 4.—Ward carriage equipped for morning baby care.

Mothers are encouraged to nurse their babies. In not a few instances, the baby is put at the mother's breast in the delivery room, as soon as the repair of the episiotomy or laceration is completed, and the parturient has been cleansed and made comfortable. This placing of the baby with the mother seems to be a considerable solace to the wailing newborn infant, gives the mother an excellent chance to see and fondle her newborn, and provides the first instruction in the technique of breast nursing.

Subsequently in the wards the babies are placed on a "demand" feeding regime. Mothers are instructed to nurse their babies for not more than five minutes during the first two or three days and as frequently as the baby seems hungry. In some cases where the baby seems unusually hungry or thirsty, a bottle of sterile lactose water is provided and administered by the mother from time to time. When the milk comes in, the mother then nurses the baby the usual fifteen to twenty minutes, and ultimately the nursing schedule settles down to about every three or three and one-half hours, depending on the requirement of the individual baby.

As the reader may surmise from the foregoing, early activation of the mother and breast feeding on a demand schedule adapt themselves very well to the program of rooming baby with mother; and in turn, the rooming-in program hastens involution and recovery of the mother, and generally stimulates more efficient breast nursing.

Most of our normal parturient ward patients are discharged on the fifth or sixth day post partum. There have been none returned to the department because of delayed post partum bleeding, subinvolution, or birth tract infection.

On the ward service, the husband is permitted to see the baby within an hour after delivery and then visit his wife and baby on two evenings a week. No other visitors are permitted except in case of grave illness or unusual circumstance. All visitors wear gowns while in the wards. The patients in the low-cost, semiprivate ward are permitted to have visitors twice a day, but this includes only the husband and mother of the patient. While visitation is always a problem, when the baby is housed with the mother, the family seems a trifle more understanding and cooperative than when the baby is kept in the central nursery, and the mother—having the companionship of her baby—is less desirous of having a large number of visitors.

Upon discharge, the mother dresses her baby in the presence of the nurse, checks the identification tags, and receives her final instructions, formula, and reference card to the Well Baby Clinic, or private pediatrician.

Reasons for Undertaking the Project

Our principal reasons for undertaking this project were two: first, the fear of contagious disease of the newborn in the central nursery, infectious diarrhea, impetigo, and respiratory infection. Unfortunately, we have had our share of these in Philadelphia and other cities of Pennsylvania, and the memory of them was fresh in our minds.

The second reason was the impossibility of maintaining a sufficiently large corp of trained nurses to care properly and safely for babies night and day. We could not satisfy our own peace of mind on this score nor could we meet the demand of the Department of Health. The procedures of central nursery care had become so exacting that under the stress of overwork and underhelp, technique would be broken here or there and the whole top heavy structure would collapse.

In addition to these two primary considerations, we were conscious of the fact that the modern hospital routine was separating the baby more and more

from its mother, and whatever the psychic effect of this separation might ultimately be on mother and child, we were certain that we were destroying a natural and very normal relationship between the mother and her offspring.

Results

It would be unwise to draw conclusions categorically on the basis of this brief nine months' experience. However, there are certain results that have impressed us as having possible significance. First as regards the health of the newborn.

In the 1,018 full-term babies housed with the mother, there have been no cases of diarrhea or impetigo and only one case of mild (questionable) respiratory infection. In the latter instance, the baby was isolated for two days because the mother had a fever following the delivery and the nurses thought the baby had a beginning upper respiratory infection. Examination by the pediatrician failed to confirm this diagnosis and the baby developed no further symptoms.

We are quite conscious of the fact that this fortunate state of affairs will not continue indefinitely and that sometime a baby in one of these wards will develop diarrhea, impetigo, or respiratory infection. If such a thing occurs, however, we know that we can immediately isolate the affected baby, that the other five babies of the ward room will have been only distantly exposed, and that the ward room can be closed to further admissions until all contained mothers and babies are discharged and the space is cleansed. This should offer quite a favorable contrast to the old arrangement in which thirty or more babies in a nursery are exposed to the infection of any one of them.

There have been no really disturbing reactions in the baby at the bedside of the mother. Occasionally a baby will choke with milk after breast or bottle feeding. As she has been instructed, the mother turns the baby on the side, pats its back, and calls the nurse. We are of the impression that the mother detects these disturbances much earlier in the baby at her bedside than do the nurses in a large nursery.

In addition to these considerations which have to do with the health and safety of the newborn, we have noted that these babies, lodged at the bedsides of their mothers, seem to be happier and more contended (if happiness and contentment can be assayed at such an early age) than they were in the nurseries. If a baby starts to cry, the mother reaches over and pats it, inspects its diaper to see if it needs changing, and nurses it if it is hungry. All attending obstetricians, nurses, and visitors are surprised at the quietness of the wards. There is nothing that even remotely approaches the pandemonium of a nursery during the late interval of a third or fourth hour feeding schedule.

Our second major consideration was as to how the rooming-in plan would affect our preconceived ideas of nursery care and distribution of nursing time. The observations on this score are of particular interest and possibly of considerable importance. Once we had the necessary equipment for individual treatment, the change from nursery to bedside care was made without a particle of difficulty. Thus far we have made no change in the traditional assignment of nursing activities—labor and delivery room, nursery, floor duty, formula room, out-patient department. The girls on nursery duty still have charge primarily of all babies: those in the premature nursery, the few in the central full-term nursery, and the babies at the mother's bedside. It is they who make the ward rounds in the morning and check the babies periodically during the day. The nurses on general floor duty during the day and night, however, are instructed to help with the incidental problems that occur in the mother and baby during the interim, and in this respect the lines of duty are not drawn as rigidly as before.

The most significant observation that has come out of this nurse-patient adjustment is the fact that with the same number of nurses and nursing hours, which under the old system was grossly deficient as regards the regulations of the Department of Public Health and our own desires in the matter, we have been able to set up in the rooming-in plan care which is adequate and very satisfactory.*

Two circumstances have brought about this improvement in care. First, early ambulation has made it possible for the normal parturient to care for herself after the first twenty-four hours, and parenthetically, to benefit by activity and leave the hospital in better condition than ever before.

Second, the rooming-in plan has made it possible for normal parturients to take over the routine care of the normal full-term baby soon after delivery. With this arrangement, nursing care is concentrated upon the ill mother, the recently born baby, the premature baby, for all of whom the hours of nursing care have been built up to an adequate level.

With the mothers participating, the hours of observation and individual care of the normal full-term baby have been increased to practically twenty-four hours in the twenty-four, and the attention given to the baby by its own mother during the twenty-four hours is as meticulous as that which would be rendered by a graduate nurse assigned to each individual baby. (Speaking for myself [Montgomery] I may say that for the first time in many years I can see a solution for the problem of adequate supervision and care of the newborn in hospital practice.)

Breast feeding is an important part of the rooming-in of baby with mother. The procedures of bedside care are naturally simplified by the mother's nursing the baby, and the demand schedule of nursing has effected earlier and steadier weight gain. The presence of the baby in the room also seems to arouse a desire to breast feed the baby in patients who had been reluctant to do so. Eighty-three per cent of the ward patients have been nursing their babies in whole or in part on the fifth or usual day of discharge, and twenty-five per cent of their babies have regained their birth weight by this time. Fifty to sixty per cent of the patients in the low-cost, semiprivate rooms nurse their babies.

As to the persistence with which this breast feeding was continued, the following data are available: Of 689 babies discharged between September, 1947, to February, 1948, 335, or roughly 50 per cent, were brought to the Well Baby Clinic of the Pediatric Department. (The remainder were referred by visiting nurses to neighborhood Public Health Centers.) Of these 335, 52 babies had been placed on a formula in the hospital or had discontinued breast feeding sometime during the first month of life. An additional 26 babies had been kept in the premature nursery for varying periods of time and discharged on artificial feeding. Therefore, of the 209 full-term babies of *this* group followed in our own clinics, 83 per cent were still nursing at the breast for one or more months after delivery.

The last question which arises in connection with the rooming-in project is, how do the mothers like it? How much benefit do they obtain from it? Under the circumstances of the ward service, the patient accepts the regime which is established by the hospital administration unless some peculiar condition necessitates an exception in the individual case. However, most of the ward mothers take to the situation with more interest and enthusiasm than a mere compliance. They appear to enjoy the companionship of the baby, manifest some degree of

*Note.—The regulations of the Board of Health of the State of Pennsylvania require that 2½ to 3 hours of nursing care be provided for each baby per 24 hours, or about one nurse to every 7 or 8 babies. The same regulations require that each mother be provided with 4 hours daily of nursing care, or one nurse to every six patients. Upon a frank review of our situation during wartime and in the subsequent period of nursing shortage, we found we were providing an average of about one hour for each baby per day, and about two hours for each mother per day. With the inauguration of 8-hour general duty nursing, these hours have not much changed to the present.

pleasure and pride in its proper care, and are jealous of its interests and safety. They do not want other patients to handle their babies and they make certain that no one comes in the room without a gown. All of them learn more about the care of their babies and are in better position to take care of their own babies upon discharge than they have ever been before.

Among the semiprivate patients, the young first mothers are the quickest to realize the value of the new project to them and are the most enthusiastic. Having been up and about at an early date following delivery and having taken care of their babies in the hospital, they have no qualms about their ability to care for the newborn when they go home. This is quite a contrast to the attitude of our primigravidous patients of a short time back.

Many of the multiparas state that they are sorry that they could not have had all of their babies this way. Others, who have lost some of the enthusiasm of their early pregnancies, look upon the arrangement as an imposition. They are frank to state that they have come to the hospital to get a rest from their household duties and care of children, and the plan is little to their liking. However, even in this latter group, if the baby is moved back to the central nursery, the mother says she misses him and is greatly concerned to know how he is doing.

The factor of knowing what is going on with her baby may be one of the important considerations for the mother in the rooming-in of babies, for the instinct of motherhood is still strong in the grand multipara as well as in the primigravida. With the baby at the bedside, no longer does the mother lie awake at night wondering whose baby is crying in the nursery, what the pediatrician thinks of the progress of her child, or whether any information concerning her offspring is being withheld. Now she has the situation entirely before her. If her baby cries, she will find out why with no delay. If she has questions for the pediatrician, she can ask them while he is examining the baby in her presence. She will know all the reactions and characteristics of her baby before she bundles him up and starts for home.

Perhaps it is not superfluous to state that the rooming-in of the babies has not interfered in any respect with the work of the obstetrician. As a matter of fact, with the two patients together it gives him a more complete picture of the mother-baby relationship and puerperal progress. He makes his rounds as usual and attends the antepartum and intrapartum patients as before. The pediatricians are more than pleased with the progress of these babies, the absence of infection, the excellent care of the newborn and the apparent contentment of the newborn, and the high percentage of breast feeding.

Just how successful the arrangement of rooming-in of babies will prove in the case of private and semiprivate patients in our hospital remains to be seen. A few patients who have desired their babies with them have been granted the privilege, although the special equipment used in the wards was not available. These mothers have expressed the same satisfaction and pleasure over the arrangement as the patients in the wards.

Feeling that the procedure is sound, we are securing the few essential articles of equipment that are necessary to make this arrangement also accessible to the occupants of private and semiprivate rooms. We foresee problems and difficulties but believe that these can be surmounted.

Summary

A system of baby care by the mother, in which some 1,018 babies, ward and semiprivate, have been housed with the mother, has been presented.

This system has satisfied the requirements for which it was set up, i.e., there have been no ill babies among these housed-in babies, and there have been no

epidemics among the newborn. The care of the baby has also been simplified and there has been no addition of nursing hours.

The babies have seemed to be contented and happy under this arrangement, have gained rapidly in weight, and the percentage of breast feeding has increased.

The mothers have in general enjoyed having their babies with them. They have learned to take care of the baby from the first postpartum day on and have left the hospital quite capable of managing the ordinary problems of infant care.

The arrangement of housing baby with mother has been found to depend for its success to some degree upon early ambulation and breast feeding, and, in turn, the housing-in arrangement aids in involution and encourages breast feeding.

The plan also seems to work particularly well in small wards where mothers can watch each other, teach each other, and can be under the frequent observation of the nursing personnel.

The question of how well this plan will work in the private and small semi-private rooms has not been adequately answered. However, we see no reasons why the plan will not work there, too, if the proper modifications and adjustments are made.

2031 Locust Street.

Discussion

DR. GEORGE W. KOSMAK, New York City.—We have been favored at this meeting, as at all previous meetings, with a large number of eminent scientific papers. However, it seems to me that we should not neglect other phases of obstetric care and particularly such topics as that which has been so admirably discussed by Dr. Montgomery. Now in the past with more confinements in homes, it was nothing unusual to have the baby with the mother and yet when the incidence of hospital deliveries increased these elaborate methods of care kept growing which in the course of time have been demonstrated to have certain disadvantages enumerated by the speaker. It is a matter of regret that the subject has been approached so much from the negative rather than the positive side. Dr. Montgomery has carefully outlined how the new system has cut down the nursing time and has made other improvements, but it seems to me that they should be balanced with the more satisfactory relationship between the mother and the newborn baby. These babies are kept in the nursery during their hospital stay and often the mother does not see the baby unless she is nursing him, until time for discharge, whereas it is that time which should be given to the mother to become accustomed to the baby and to know what are his needs.

Another thing, many of these women get a sort of demonstration the day they leave the hospital and a lot of information is put in this short period which is necessary to be remembered by the mother. It was very satisfactory to have Dr. Montgomery state that breast feeding has been encouraged by this method because I think it is one of the great failures of our modern hospital system in the care of babies, that not sufficient breast feeding is being encouraged. I believe that is one of the most important things to be considered in connection with this new scheme. It requires very little alteration in the hospital facilities. My own experience is very limited but I have found a lack of cooperation, unfortunately, between the nurses and the patients and the doctors in attendance, and that should be eliminated.

Many women come to the hospital, after having gone through perhaps a distressing period of pregnancy, with the idea that they want a good rest. However, as Dr. Montgomery has stated, it is not really a big chore for the mother to take care of the baby's requirements. It would be very fortunate indeed, I believe, if more institutions throughout the country could develop this rooming-in system so that we could have a further trial of it.

DR. ROBERT D. MUSSEY, Rochester, Minn.—Early ambulation of the woman following delivery and housing the baby with the mother are two innovations in the generally accepted routine of postpartum care.

The authors are conservative in not drawing definite conclusions following the comparatively short trial period, although they state that they are sufficiently convinced of the value of the program to justify its further trial.

Somewhat over a year ago, Dr. Anderson Aldrich, Director of the Child Health Institute in Rochester, Minnesota, discussed "rooming-in" of the baby with the mother with the Staff of the Obstetric Department and with those in charge of nursing and administration at St. Mary's Hospital, in the hope that it would lead to a trial of this procedure in the care of the newborn in the above-mentioned hospital. Up to the present, its trial has been delayed, owing chiefly to problems of nursing and architectural arrangements.

I was interested to attend an open discussion of this subject, under the chairmanship of Dr. John Parks, at the last Congress on Obstetrics and Gynecology at St. Louis. Since then, and particularly after being asked to discuss this paper, I have become more familiar with the pros and cons of "rooming-in."

More or less haphazard neonatal care forty and fifty years ago gradually has been replaced, chiefly owing to guidance by the pediatrician, by the set regimen of baby care which still obtains. Employment of a central nursery for all well babies except those born prematurely, strictly regulated hours of breast nursing at which time the baby is carried to the mother for breast or bottle nursing has obtained on the average obstetric service; too frequently bottle feeding is done in the nursery. Under this regimen the baby is separated from the mother except for brief nursing periods amounting in over-all time to approximately one and one-half hours daily. When the baby cries, if the nursery service is adequate and alert, he is given individual attention and then must wait completion of the routine three- or four-hour interval for the next nursing period.

The newborn baby, which, during gestation is enveloped by the mother, nourished and protected by her, is abruptly separated from her at birth. Instead of that close maternal association and protection which obtains in the case of practically all newborn warm-blooded animals, the human infant is placed in an environment of asepsis, technique, and rules, removed from maternal contact and protection, except for more or less widely spaced periods of feeding.

Proponents of the central nursery system have argued that this system is more practical from the standpoint of nursing care and safe supervision of the baby, and that the routine nursing interval is of value in beginning to train the baby in regular habits.

A few years ago, Aldrich and his associates carried out for a month twenty-four-hour observation periods in the nursery during which the crying time of each baby and the apparent cause of crying were charted. It was found that the total time of crying was almost inversely proportionate to the individual attention it was possible for the nurses to give the baby. Aldrich stated that during the early weeks of life a tabulation indicated also that nursing infants select a periodic time for nursing routine, if permitted to do so. This permits a nursing schedule to be established to the individual needs of each infant.

Those who favor rooming-in present many arguments in its behalf. Time does not permit repeating all of these. The author has emphasized the danger of infectious diarrhea of the newborn as compelling evidence against the large central nursery.

Also, the proponents of rooming-in state that it assists the mother, under proper guidance, to develop her responsibility in caring for her baby, that it gives a psychological lift to both individuals in the mother-infant relationship and a return to an approximation of the relationship which obtained before the advent of the modern nursery for the newborn; it permits well-mothered infants to develop into more psychologically stable adults, and even enables the father to evaluate better his role in the infant-parent relationship and to adjust himself to it.

Many European hospitals are now using and have for many years employed "rooming-in" baby care. Rooming-in is an interesting experiment which is well worth further trial and study in this country.

Maloney quotes a Taoist inscription which says in part, ". . . he who knows how to cleanse the current of a stream begins by cleaning out the source. And he who would straighten the end of a process, must commence by making its beginnings correct."

DR. HARVEY B. MATTHEWS, Brooklyn, N. Y.—The one point I would like to make is that if an institution such as the Rotunda, which has not closed its front doors for 203 years, has used the housing-in method with entire satisfaction, it is certainly worthy of trial by us American obstetricians, particularly under present-day conditions. I think, furthermore, we have allowed ourselves to foster the establishment of central nurseries with too many frills nad foibles and that we should come "back to earth" and pay attention to what Dr. Montgomery has outlined.

DR. EDWARD L. KING, New Orleans, La.—Just a word to substantiate what Dr. Matthews has said. I have noticed that same situation in Dublin in the Rotunda and also in the Coombe Hospital. At the latter, it is carried to the full extreme and the baby stays in the bed with the mother the whole time. One of the Dublin pediatricians addressed the Conference and he said that in their three hospitals the percentage of trouble in the way of infection and diarrhea in the baby was less in the Coombe Hospital where the baby was kept in the bed with the mother. Next was the Rotunda Hospital where the baby was in a separate crib, and more trouble was found at the National Maternity where the hospital and nursing were more modern. In London, at the Queen Charlotte Hospital, they had much the same system; and in two hospitals in Paris they seemed not to have heard of a central nursery but have always had the babies with the mothers.

DR. MONTGOMERY (Closing).—Apparently the discussers, all of them, agree that there is a very salutary trend in this rooming-in project of baby with mother toward the simplification of baby care and that the more this care of the newborn is simplified and brought back under the mother's observation, the better are the results, both immediate and remote.

I would particularly like to emphasize the fact that this project requires no special or unusual architectural adjustment in the hospital maternity. Our own institution was never planned for such a project. In fact, the maternity division was built at a time in which the central nursery was considered to be quite the thing. Actually, it has cost us about $6 a crib to provide the equipment for each baby. And I think this equipment has proved just as satisfactory and perhaps more so than some of the very complicated apparatuses which I have seen for the individual care of babies in a room or in a central nursery.

I would like to emphasize the fact that these babies are getting much better care and more constant observation with the same amount, or perhaps less, of graduate nursing than before, and that we are able to use this graduate nursing to great advantage in the premature nursery and in the care of the ill baby or ill mother. With the shortage of undergraduate and graduate nurses, this is an important consideration with us and I imagine it is going to prove an important consideration elsewhere.

I have the feeling that this project is going to develop and spread throughout the country and that, as soon as the advantages, both physical and mental, to mother and baby are realized, there will be a growing demand by mothers to have their babies with them throughout the hospital puerperium.

WIDE CONIZATION OF CERVIX*

Follow-Up of One Thousand Cases, Six Hundred From Two to Fourteen Years

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THE problem of the operative treatment of extensive chronic cervicitis has taxed the ingenuity of some of the outstanding leaders in gynecology since the early part of the nineteenth century. A brief review of the main steps in working out the solution of this problem will help one to realize the difficulties encountered, and will give an historical perspective of the development of our present-day methods.

Historical Notes

Lisfranc,[1] in 1815, was one of the first to attack the problem. In cases which he presumed to be early cancer, he removed a wedge-shaped block extending from the vaginal margin of the cervix up to the internal os. This wound was allowed to heal by granulation over a period of five to six weeks. These patients were usually treated in the hospital for four to six months before operation was attempted. Later investigation demonstrated that these cases were not cancer but chronic inflammation with induration and hypertrophy of the cervix.

In 1860, J. Marion Sims[2] credited Huguier, of Paris, with performing this operation oftener than any other surgeon, and states that he (Sims) and Emmet had used the method frequently; but Sims found that the prolonged period of granulation resulted in dense strictures which could not be relieved by repeated incisions or other methods of dilation.

In attempting to improve the operative treatment, Sims first tried splitting the cervix transversely nearly to the vagina and then amputating in such manner that a conical excavation with apex upward remained. The strictures were just as persistent with this type of operation, even when he did it in two stages, removing the anterior and posterior lips a month apart. He then revised the technique further, stating, "I removed five-eighths of an inch of the cervix, cutting at right angles and within half an inch of the vaginal insertion. On beginning the operation, I intended to leave the cut surface to heal by the granulating process, which usually takes five or six weeks, but while sponging the wound and waiting for the hemorrhage to cease, I discovered that the stump could be covered over with healthy vaginal tissue in the same manner that a stump of an arm or a leg is covered after amputation by the circular method. This was done by passing four sutures of silver wire through the anterior and posterior borders of the wound which, when tightly drawn, brought its edges into apposition in a straight line across the middle of the stump, covering it completely, but leaving a small central opening just over the outlet of the cervical canal." The sutures were removed in a week. He reported three cases in which this operation was

*Read, by invitation, at the seventy-first annual meeting of the American Gynecological Society, Williamsburg, Virginia, May 24 to 26, 1948.

used, and in all three "menstruation was easy since the operation, though the os was smaller in each than natural, and required to be enlarged by slight incisions." He concluded, "So in amputating the cervix, it is not necessary to cut it off even with the vaginal insertion to insure a good result, for whatever is left will be decreased by a modified nutrition, just as we see after amputation of the arm or leg."

Thomas Addis Emmet[3] was the first to emphasize clearly the importance of laceration as the underlying cause of eversion, erosion, and chronic cervicitis. He devised a plastic operation in which the lateral portions of the affected surfaces were freely denuded, leaving in the center of each lip an undenuded strip which formed the continuation of the uterine canal to the external os. By 1874 he had performed this trachelorrhaphy operation nearly two hundred times, with ultimate benefit in most cases. In discussing Emmet's paper, Sims stated, "I have performed the operation often enough to speak in positive terms of its value. The discussion of the subject must of necessity be one-sided. There can be no objection, no opposition to the operation. We must accept it as Dr. Emmet has given it to us. We can't modify the operation; we can't change it; we can't improve it; it is perfect: perfect in method and perfect in its results. We owe Dr. Emmet a debt of gratitude for this valuable contribution to uterine surgery." Incidentally, this and other free exchanges of credit indicate the unselfishness and high character of these two great pioneers in gynecology. In regard to this particular operation, however, the results of leaving part of the diseased tissue as the central undenuded strip became evident under later critical observation and analysis of results.

In order to secure the benefit of complete excision of diseased tissue and yet avoid the difficulties following regular amputation, various modifications of amputation were made by a number of workers, including Schröeder,[4] Bonney,[5] and Kelly.[6] In 1913, Leonard[7] made an excellent statistical analysis of the postoperative results in cases of amputation of the cervix done in the preceding twenty years in the Gynecological Clinic of the Johns Hopkins Hospital. There were four hundred cases but he was able to obtain complete protocals in only 128. He states, "The results were quite unexpected and in many ways disappointing." In regard to postoperative bleeding, he found that the dangers from serious hemorrhage after amputation were very real. Many of the cases required tight packing and five per cent of the cases bled so profusely at some time during the convalescence as to require removal to the operating room for resuture of the cervix.

In an article the following year, Leonard[8] compared the results of amputation with those of trachelorrhaphy. In his series of trachelorrhaphy cases there was no serious bleeding and only six cases required a light pack. In ten first-child deliveries after trachelorrhaphy, only one was difficult; whereas, in eleven deliveries after amputation, seven were difficult. But in regard to cure of the cervicitis with its leucorrhea, he found trachelorrhaphy undependable and concluded that "although trachelorrhaphy may render mild cervicitis more amenable to treatment, it cannot be considered a curative measure for this condition."

It was in 1916 that Sturmdorf[9] devised a technique which would permit removal of all of the diseased tissue and yet not complicate future labors. The steps in this procedure were: 1. Outlining and free mobilization of an ample circular flap from the vaginal coat of the cervix; 2. Complete excision of the entire cervical mucosa to the internal os; 3. Sutural coaptation of the vaginal cuff to the denuded cervical cavity. After critical test of results over a period of three years, he found that the operation fulfilled the requirements for which

it was designed; namely, it eliminated the diseased portion of the cervix, preserved the normal arrangement and contour and function of the cervical musculature, secured permanent accurate coaptation of flap to stump, and obviated the extensive scar tissue stenosis which had caused serious labor complications after amputation.

Harvey Matthews[10] in an instructive analysis of two hundred cases of Sturmdorf operation, followed six months to three years, found 64 per cent were cured, 28 per cent were improved, and only 8 per cent were failures. He stated that, while the method was not a perfect one, it was the best so far devised for eradicating the infected area, and that it caused no more trouble with subsequent labors than did the required extensive trachelorrhaphy. In England, John W. Burns[11] analyzed the results of the Sturmdorf operation in ninety-two cases followed for two to three years. He found that only three cases remained uncured, and two of these had had gonorrhea. Of the ten full-term pregnancies, all had normal deliveries.

In spite of the various painstaking analyses showing the deficiency of trachelorrhaphy, this incomplete operation continued popular, presumably because the alternates (amputation and Sturmdorf) were more formidable and the smaller operation did effect satisfactory relief in many cases in which the inflammatory infiltration was largely lateral. In the discussion of a paper by Polak[12] in 1923, John G. Clark, Brooke M. Anspach, C. P. Noble, F. E. Keene, and Richard Norris still felt that trachelorrhaphy was preferable.

An excellent compilation of the results of trachelorrhaphy, amputation, and the Sturmdorf operation was made by Pendleton Tompkins[13] in 1935. In addition to summarizing many series of reported cases, he gave the results of his study of 611 cases done at the University of Pennsylvania Hospital. From this comparison of the results of many operators, the statistics showed cures by trachelorrhaphy in 70 per cent, by Sturmdorf operation in 80 per cent, and by amputation in 83 per cent; but when the difficulties in labors subsequent to amputation are considered, the Sturmdorf procedure is decidedly the preferable operation of the three.

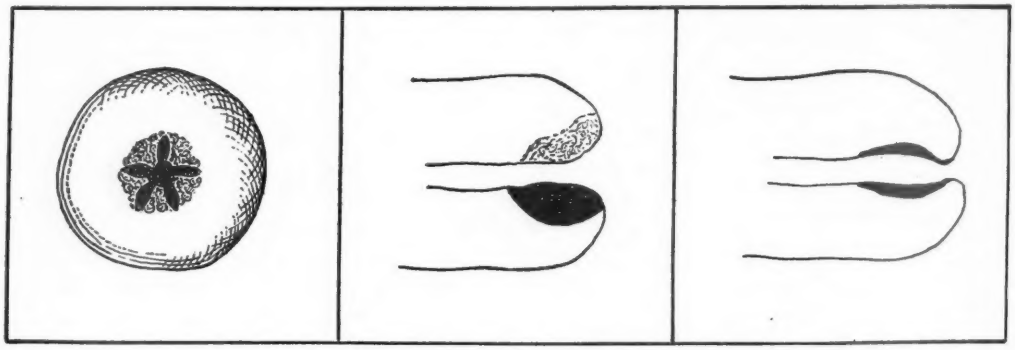
Deep coagulation by the high frequency current (and its predecessor, deep cauterization) have had quite a run of popularity alongside the other measures mentioned, and coagulation is still advocated by a considerable number in this country and abroad. However, it has some very undesirable features. W. T. Black,[14] in a review of results of treatment of cervicitis, reached the conclusion that the dead, odoriferous slough which remains for some time after coagulation is followed by hemorrhage, by inflammatory complications including pelvic abscess, and by stenosis more frequently than is found after other cervix operations. A very serious obection to coagulation is that it precludes microscopic check of the removed tissue. This chronically irritated tissue may harbor beginning malignancy, and an important feature in the handling of chronic cervicitis is removal of the affected tissue in such a way as to permit microscopic investigation of every part of it. Removal of a specimen before coagulation is not sufficient, for the early carcinomatous cell change may be in another area.

It is not necessary to labor the point that chronic cervicitis is a factor in the causation of cancer. The voluminous literature on the subject has long since established that fact and shown the imperative need of prompt removal of this chronically irritated tissue—if possible before carcinomatous change develops, and most certainly in a way that will permit of thorough microscopic investigation. Incidentally, in connection with the long search for the relationship of cervicitis and other factors in the causation of cancer, it is interesting to note the theory recently presented by Ayre[15]; namely, that chronic irritation in the cervix causes a local excess of estrogen, which unduly stimulates growth, and

a deficiency of thiamine and riboflavin, which control normal mature development—hence, the forced growth is toward embryonic cells and in certain patients toward malignant change. If this theory is substantiated, it will constitute another reason for prompt removal of chronic cervicitis.

Concerning the prevention of cervicitis, with its cyst formation and eversion and extensive inflammatory infiltration, the importance of primary repair of cervical tears has been stressed by Bubis,[16] Emge,[17] Polak,[18] Farrar,[19] and others.

As to office procedures in chronic cervicitis, linear cauterization with the nasal tip (Fig. 1), first advocated by Dickinson,[20] has long been accepted as an excellent method of curing mild erosion and eversion. A more recent addition to office procedures for these mild cases is the endocervical conization introduced by Hyams.[21]



A. *B.* *C.*

Fig. 1.—Linear cauterization of the cervix. *A*, showing the cautery incisions, and also the type of lesion suitable for this treatment; *B*, showing the deepening of the cautery incisions on the inside, so as to secure inversion from the scar contraction; *C*, indicating the satisfactory overcoming of the eversion, by the drawing-in effect of the inside scars.

Mortimer Hyams did a splendid service for the profession when he presented the principle of conization for endocervicitis. The presentation was made in 1928, and was followed by other papers giving his further experience with the method. The general arrangements for conization are shown in Fig. 2, and the shape and size of his electrode and its position in the cervix are shown in Fig. 3, both illustrations being from his paper. Hyams' object was to remove the endocervical mucosa. He shaped his electrode accordingly, and it accomplished the purpose admirably. He insisted that the removal of tissue should be limited to that within the canal and to the 1/8-inch width of his electrode.

Wide Conization

In the handling of chronic cervicitis cases, I became convinced that a wider excision would permit a cure of the extensive cases by conization. In a large proportion of the cases, the inflammatory process and cyst formation has extended beyond the endocervical mucosa out onto the vaginal surface of the damaged cervix and into the underlying deeper tissues. For removal of this widespread area of affected tissue, a larger electrode of different shape was needed, so I took up the problem.

Not being able to find the type of electrode needed, in a search of catalogues and in communication with various diathermy companies, I made sketches

of several types desired for trial. The High Tension Company of New York offered to make up some according to the specifications on my sketches. After experimenting with different types, I found that the type shown in Figs. 4 and 5 best accomplished the work desired; namely, complete removal of the affected

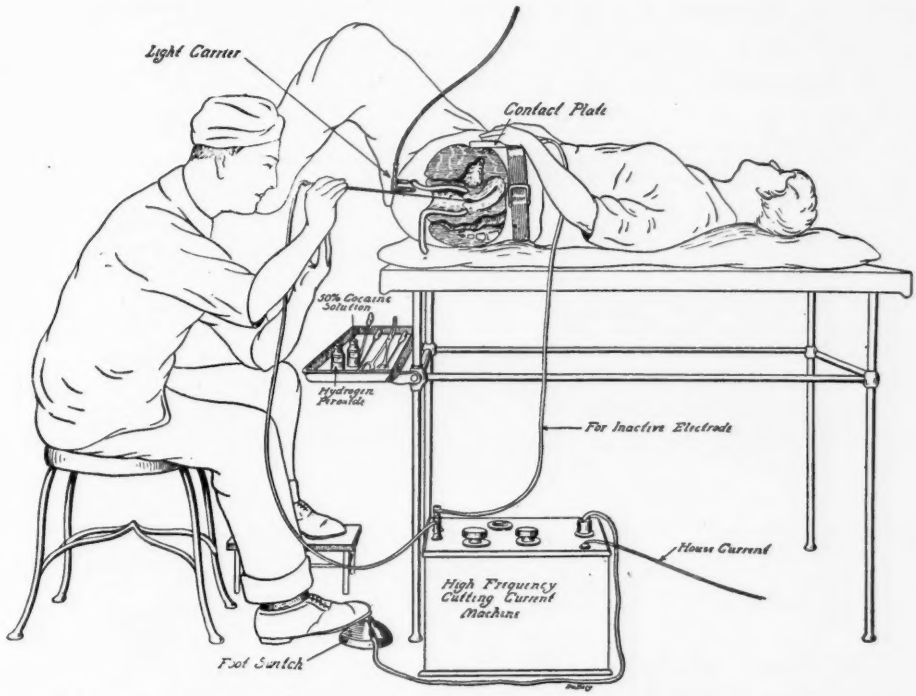


Fig. 2.—Schematic drawing of surgeon and patient during conization. (Hyams—*Am. J. Obst. & Gynec.*)

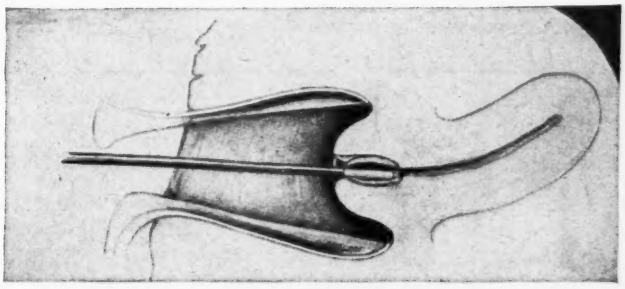


Fig. 3.—Hyams electrode in cervical canal. (Hyams—*Am. J. Obst. & Gynec.*)

tissue in extensive cases. I had in mind calling this a modified Hyams electrode, as it merely extended the application of the hemostatic-cutting current excision. But in his article Hyams had strenuously objected to having any electrode called a modification of his if it did not conform to his original specifications. Obviously, an electrode for this wide conization must depart radically from those specifications.

After devising the electrode and securing its manufacture in 1933, it was subjected to extensive clinical testing, not only by myself but also by other gynecologists. After its use in eighty cases by sixteen members of the Gynecological Staff of Washington University and Barnes Hospital, the new electrode was reported in 1935.[22] As more experience was gained with the technique, we extended wide conization to cases which were still more extensive and in which we were still using the Sturmdorf operation, and found that this extremely wide coning by the electrode worked well.

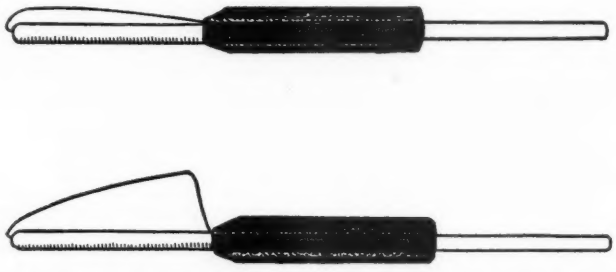
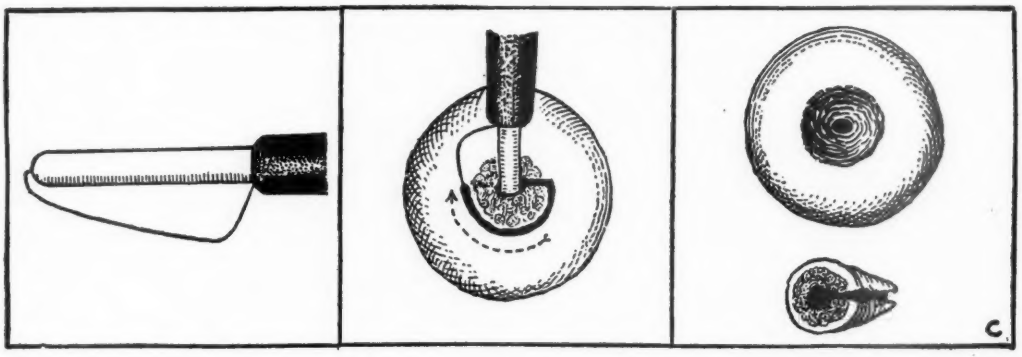


Fig. 4.—Upper electrode a Hyams, wire is one-eighth inch from the central core. Lower electrode is a medium-sized Crossen used for the wide conization to include all of diseased tissue. (Crossen—*Am. J. Obst & Gynec.*)



A. *B.* *C.*

Fig. 5.—*A*, The new electrode for wider conization.

B, Indicating the method of using the electrode, i.e., a wide excision taking in all the affected area.

C, The excised cone of tissue; also the remaining funnel-shaped cavity, which heals rapidly with good inversion. (R. J. Crossen—*J. Missouri M. A.*)

In the early work with this electrode, bleeders were coagulated with a ball electrode or with the wire, but it was found that these were the cases which gave trouble with delayed bleeding. We were reluctant to place sutures to control bleeding, for we did not know then whether the approximated coned surfaces would heal. However, by observing the occasional case in which bleeding necessitated suturing, we found that the healing progressed normally. For a considerable time suturing was limited to cases with active bleeding or to cases with associated radium treatment for myoma or dilatation and stem for dysmenorrhea (experience having shown that postoperative removal of a tube or

stem tended to loosen the small coagulation clots and favor bleeding). When the conization was exceptionally wide, a Sturmdorf suture, front and back, was used to draw in the flaps.

In 1939,[23] Dr. George J. L. Wulff and I reported three hundred cases of wide conization done by various members of the Washington University Staff. In that paper we reported also an improvement of the original electrode by Dr. T. K. Brown. He had the central metal core covered by an unbreakable lucite insulator instead of the very fragile one of porcelain previously used. Also, the nichrome wire was arranged so that it could be replaced easily and the loop size could be adjusted as desired for different electrodes. Fig. 6 shows the improved electrode and also the two sizes most frequently employed, the width of the larger being 5/8 inch, and of the smaller, 3/8 inch. The length of the cutting part is 1¼ inches.

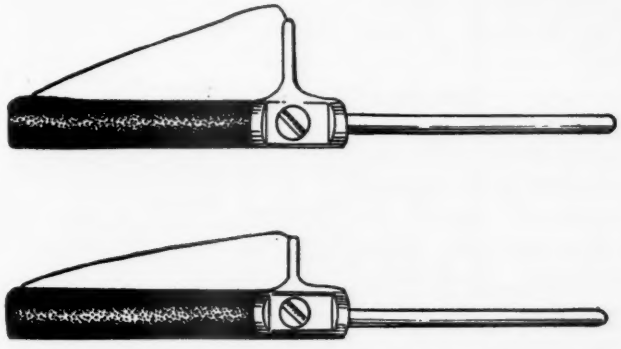


Fig. 6.—T. K. Brown modification of Crossen electrode. The unbreakable central core and replaceable cutting wire increase the durability of the electrode and reduce repair costs. (Crossen—*Am. J. Obst. & Gynec.*)

The method of relining the coned area is shown in Figs. 7 and 8—first a Sturmdorf suture front and back to draw in the flaps, then a superficial stitch or two on each side to turn in any everted edge, and then a tube in the canal to prevent healing across the canal and to guide epithelization. Though many cases will get along satisfactorily without the tube, we have come to use it routinely as a precaution. It should be of fairly small size so as not to make sufficient pressure to interfere with epithelization, and should have a T-piece on each end to prevent slipping down into the vagina or up into the uterine cavity, which has happened at times. Also, as with all pelvic or abdominal drainage tubes, it should be of red rubber, which is opaque to x-rays and, therefore, can be identified if lost in the uterus.

Wide conization was designed to accomplish and does accomplish certain important things for the patient:

1. It removes the extensive chronic cervicitis thoroughly, even though the process extends far out on the vaginal surface of the cervix and deeply into the tissues beneath. When there is associated old laceration with inflammatory swelling and eversion, there is produced the distorted infiltrated cervix for which trachelorrhaphy was formerly the accepted operative treatment. Trachelorrhaphy failed to remove all the diseased tissue, because a central strip on

each side was left to form the new canal. Wide conization removes all the diseased tissue, and the turned-in flaps give an epithelial lining to the canal. Comparing it with the Sturmdorf operation, wide conization with the hemostatic-cutting wire does all that the admirable Sturmdorf operation did without the profuse bleeding and hurried hemostatic measures which were a normal part of the latter operation.

2. It removes all of the affected tissue in condition for microscopic examination. In this respect it has revolutionized specimen-taking from the cervix. Formerly, the custom was to remove a small specimen from the most suspicious area of the cervix, and if this did not show malignancy, to wait until another area began to look suspicious of malignancy and then remove a small specimen there—oblivious to the facts (a) that there may be in any part of the affected area beginning carcinoma which does not yet look suspicious, and (b) that while the physician is waiting for suspicious signs, an early carcinoma may be making serious progress. Now, when chronic cervicitis is present, all of the affected tissue is removed by wide conization, and all is subjected to critical investigation in the laboratory. This settles at once and definitely whether or not there is beginning cancer.

Details of Handling Cases

Before going into the tabular analysis, I should like to describe briefly our usual way of handling these cases. For some time prior to the operation the patient uses an acid douche to improve the vaginal pH and flora. Before the war, when it was possible to select a time for the operation, the conization and curettage were scheduled for shortly after the menstrual period. The patient enters the hospital the day before operation, and a vaginal instillation of 1 per cent neutral acriflavine in glycerine is made as soon as convenient, and again the morning of operation, and again immediately after completion of the operation.

At operation, an electrode of suitable size is selected and the cervix is coned as shown in the illustrations. Occasionally it was found that a deeper cyst was opened but not removed in the first round, in which case the remaining area of affected tissue was removed by additional use of the cutting wire. However, it is well to avoid additional use of the cutting wire when practicable, by including all the affected area in the first round, the cutting wire being directed through healthy tissue with a good margin between it and the disease. Also, it is important to regulate the current so that it cuts as rapidly as is consistent with hemostasis, for slow cutting widens the narrow coagulation line and may damage an adjacent part of the specimen.

After the infected tissue is all removed, we place an anterior and posterior Sturmdorf suture to turn in the flaps. In doing so, we do not use the mattress-type bite in the lip as originally described by Sturmdorf, for in our experience the simple single bite, as shown in Fig. 7, turns in the squamous edge better than did the mattress type. In some of the early cases we tried undermining the vaginal mucosa, thinking to secure better coaptation of the flaps, but we soon discovered that the free bleeding nullified the advantage of the hemostasis obtained by the use of the cutting current; also, follow-up of the cases not undermined showed the ultimate result was excellent. One or

two superficial lateral sutures close any open area at the sides and then the tube is introduced. The small soft rubber tube with a T-piece on each end is placed with the upper end just within the internal os. This is removed just before the patient leaves the hospital, which is on the third or fourth postoperative day.

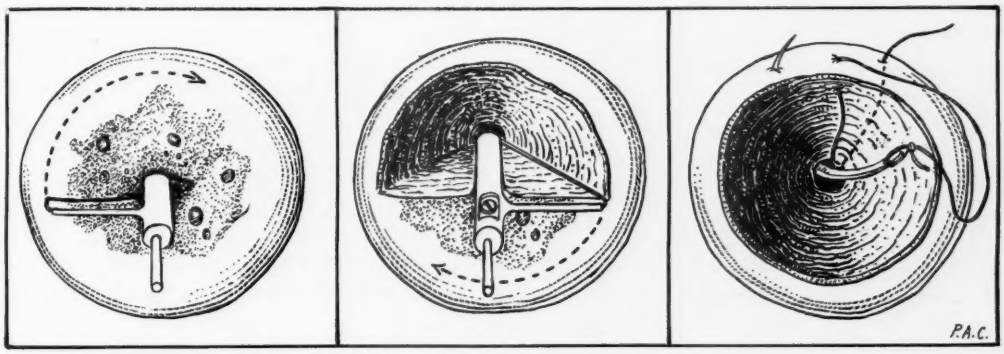


Fig. 7—Extensive conization with modified Crossen electrode, showing use of Sturmdorf suture on anterior and posterior lips to aid inversion during healing.

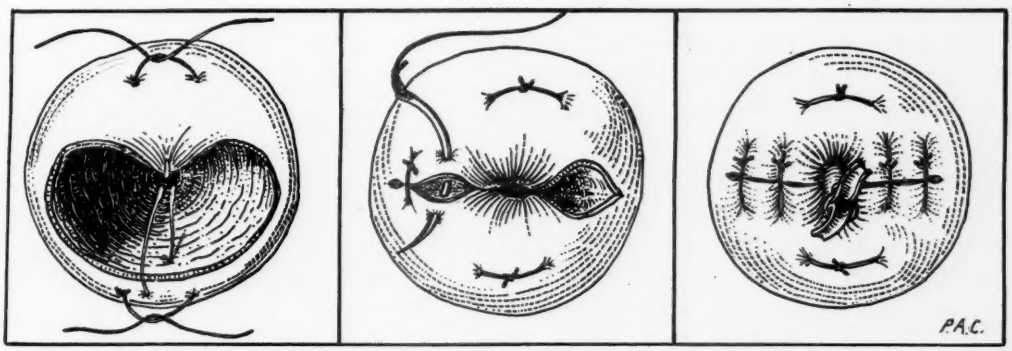


Fig. 8—Shows lateral sutures and completed procedure with the T tube in place.

On discharge from the hospital, the patient is instructed to take a daily lactic acid douche or vinegar douche. If there has been a definite vaginitis prior to the conization, an acid jelly or triple-sulfa jelly is advised in addition to the douche. When the patient returned to the office in four to six weeks, we formerly passed a small sound through the internal os to make sure there was no stricture, but we found that this was not a reliable test for stricture, for it is often difficult to pass a sound through the internal os of a normal cervix which has not been operated upon. At present we pass a sound only in cases where there seems to be some narrowing of the external os or cramping with periods or marked decrease in the menstrual flow.

Wide conization for extensive chronic cervicitis is a hospital procedure. Curettage also is needed in a large proportion of the cases as a therapeutic or diagnostic measure, and deep accurate palpation of the pelvic interior under the

anesthesia is needed to exclude silent ovarian carcinomatous infiltration. If the patient has a myoma with bleeding, the myoma activity can be stopped by a suitable dose of radium at the same time, and the curettage will exclude complicating endometrial carcinoma. All this is accomplished with a short hospitalization and anesthesia, and the patient goes home with the chronic cervicitis removed and with her mind free from anxiety as to something developing in uterus or ovaries.

The importance of taking advantage of the short anesthesia to do a curettage along with the conization is emphasized by the fact that this associated curettage revealed early endometrial carcinoma in eight of these patients. This point is still further emphasized by our experience in a series of myoma-radiation cases.[24] In the 549 myoma cases selected for radiation treatment, the preliminary curettage revealed endometrial carcinoma in 23 of these women. Incidentally, in this series of myoma-radiation cases, there were 233 conizations for chronic cervicitis along with the radium treatments for the myomas, giving abundant opportunity for observing the combination, and it worked well.

Since the introduction of wide conization in 1933 as previously described, and the published report in 1935, several series of cases have been reported by other gynecologists. Comparing certain features of the other reported series with the details of our present technique brings out some interesting points. In regard to control of bleeding, spot-coagulation is recommended by Norman Miller and Todd,[25] T. K. Brown,[26] J. J. Haber,[27] M. A. Roblee,[28] and M. L. Stadiem.[29] We started with spot-coagulation but our experience, previously detailed, caused us to adopt suturing, and we feel strongly that the routine suturing turns in the flaps better and gives more secure hemostasis without the small coagulation sloughs which favor secondary hemorrhage, particularly when a tube or stem is to be removed from the canal. The routine suturing, as shown in Figs. 7 and 8, has practically eliminated bleeding, and also hastens healing by accurately approximating the coned surfaces.

Routine postoperative dilatation when patient returns to office is advocated in most reported series. We felt at first that this was advisable, but with increasing experience decided that in many patients it was not needed, that the sound-test was often misleading as to a normal internal os, and that it was best to leave the internal os undisturbed unless there was evidence of trouble there.

In regard to the effect of conization on subsequent labors, Miller concludes that "In general, conization should be limited to women past the childbearing age." Roblee states, "Although we practice and teach that conization should not be performed during the active childbearing age, there is little clinical evidence in our hands to support this conclusion." Brown states that conization "will not interfere with subsequent pregnancies nor complicate future deliveries."

In our experience there was no evidence that conization caused trouble in subsequent labors.

Conization was frequently associated with other operative work. In the series, there were 267 associated radium treatments for myoma or delayed menopause, 119 abdominal operations, 116 vaginal plastic operations, and 32 com-

bined abdominal and vaginal operations. We experienced no trouble from the combination of other operations with conization, except in an occasional case of radium treatment for myoma in which the radium extended to the internal os instead of being placed well above it. Particularly helpful is conization for any cervicitis in the cervical stump left while doing a hysterectomy which must be supravaginal instead of complete.

Analysis of Cases

The present study is an analysis of 1021 cases of wide conization for chronic cervicitis from the private practices of H. S. Crossen, R. J. Crossen, and George J. L. Wulff. The periods of observation are shown in Table I. We feel that the group is large enough and the cases have been followed long enough to permit drawing reliable conclusions as to the effectiveness of this method of treatment. The questions in our own minds which we sought to answer were:

1. Does wide conization with suture heal as well and give as good ultimate results as the Sturmdorf operation?
2. In how many cases did postoperative bleeding or later stricture occur?
3. Were subsequent deliveries complicated because of the conization?
4. In how many patients did the wide conization for cervicitis lead to an early discovery of cancer?
5. Did conization reduce the incidence of subsequent cervical cancer?

In the first place, the wide conization for chronic cervicitis and the associated curettage revealed early carcinoma in 16 of these patients (8 cervical, 8 endometrial), which, of course, removed them from the cervicitis class to treatment for cancer—leaving 1005 patients to be followed to determine the results of conization in cervicitis.

The follow-up of these patients was by examination in our office for 542, examination by other physicians for 105, and by questionnaire for 358. The questionnaire asking the following: (1) Have you had any troublesome discharge? (2) Have you had any later pelvic operation? When? What was done? (3) Have you had any pregnancies? Give number and outcome. (4) Have you had a pelvic examination since I last examined you? Was the pelvis found to be in good condition?

When a patient did not answer the questionnaire, her last office visit then constituted the end of her follow-up. Conization patients who did not have a checkup after leaving the hospital were not included in the series.

In order that our statistics could be completely unbiased, we asked Dr. A. C. Trueblood, who had nothing to do with the treatment of these cases, to obtain the information from the histories. We wish to take this opportunity to exress our appreciation for his valuable contribution in carrying out this part of the work.

As seen in the figures on age grouping, nearly half of the patients were in the childbearing age.

Comparing this series of patients who had wide conization with reported series of the Sturmdorf operation and with our own work with the latter operation, we find that the conization wound made with the cutting current heals as

satisfactorily and the ultimate results are as good as with the excellent Sturmdorf operation and without the free bleeding and hurried hemostatic measures which constitute a normal part of the latter operation. The items of particular interest in such a comparison are: postoperative bleeding, later stricture, conditions requiring additional treatment or reoperation, and effect on subsequent deliveries.

In this series of conizations, there were only eleven cases in which postoperative bleeding occurred, and in none of them was it severe in character. In one of the eleven cases the bleeding was not from the cervix but from the endometrium, and was stopped by curettage. In each of the other ten cases, the bleeding was controlled by a single tamponade.

There were 16 subsequent strictures in this series, the severity of the cases and required treatment being shown in Table II. Twelve of the strictures occurred within the first year after the conization, and the remainder within the first five-year period.

TABLE I. PERIODS OF OBSERVATION AND AGES OF PATIENTS

Less than one year	259
One year	112
Two years	83
Three years	74
Four years	70
Five years	44
Six years	46
Seven years	40
Eight years	44
Nine years	45
Ten to fourteen years	188
Total	1005

AGE GROUPING OF WIDE CONIZATIONS

16 TO 39 YEARS		40 AND OVER	
NUMBER	PER CENT	NUMBER	PER CENT
436	43.4	569	56.6

TABLE II. STRICTURES, SHOWING TIME AFTER CONIZATION, AND TREATMENT

TREATMENT FOR RELIEF	NO.	TIME AFTER CONIZATION			DYSMENORRHEA PREOP.
		UNDER 6 MO.	6 MO.-1 YR.	2 YR.-5 YR.	
Office treatment, dilatation, stem or tube	13	9	1	3	3
Operative treatment	3	1	1	1	2
Total	16	10	2	4	5

In Table III are shown details of the fourteen cases requiring reoperation under anesthesia. In three of these, the later operation was for stricture, and one also had complicating pyometra. In the other eleven cases, there was a reconization or excision of the cervical stump for cervicitis, which was either persistent from time of conization or a new development following labor or infection. In three of the eleven cases, the cervicitis had persisted because not all of it was removed in the primary conization. In the remaining eight cases, the patients had been well for five years or more, a fairly clear indication that the local inflammation was a new development. Three of these eight patients had intervening pregnancies, and one had been delivered three times since the conization.

In addition to the secondary treatment cases shown in the two preceding tables, there were 54 other patients for whom some minor treatment later was required to complete the cure. In 14 of these, the trouble was persistent from

the time of conization, and consisted of an everted lateral edge or some other minor defect in healing, requiring light touching with cautery. Our suturing technique of recent years, shown in Fig. 7, has almost stopped these edge eversions. Seven hundred twenty-seven cases received this suturing. The remaining 40 patients required late minor treatment for removal of polyp or puncture of a cyst or linear cauterization for a small area of erosion or eversion. We were able to check on all but eight of the questionnaire patients who answered "yes" on discharge. Those having cervicitis are included in the retreatment group, and the eight we were unable to check were counted as recurrent cervicitis.

TABLE III. REOPERATION CASES, WITH DETAILS

		NO.	1-2 YR.	2-5 YR.	6-12 YR.	
Reoperation for stricture	Plastic operation	2	1	1		(Dudley operation)
	Hysterectomy	1	1			(Also pyometra)
Reoperation for cervicitis	Reconization	10	1	2	7	
	Excision cervix	1			1	(Excision of cervical stump)
Total		14	3	3	8	

Counting the 14 cases reoperated upon and the 13 strictures requiring only office dilatation and the other 54 cases requiring some minor treatment to complete the cure and the 8 uncertain cases from the questionnaire, there were, in all, 89 cases requiring some later treatment—some for a condition persisting from the conization and some for a new development, such as polyp or cervicitis following labor or infection. In this group there were 48 cases in which our present suturing technique was not used, 36 in which no tube was placed at operation, and 11 in which a radium treatment was given in conjunction with the wide conization.

Taking up the matter of labor after conization, in our series there were 75 patients who conceived, having a total of 95 pregnancies. There were 63 deliveries at or near term, 49 of which were first deliveries following conization, details of which are shown in Table IV.

TABLE IV. FIRST DELIVERIES SUBSEQUENT TO CONIZATION

49 First, postconization deliveries at or near term	No difficulty	44		
	Difficult deliveries	4	Cesarean section. Ages 42, 39, 34, 38	Two, because of previous difficult deliveries. One, head too large. One, several indications
		1	Difficult forceps delivery	Four previous difficult deliveries, all over 10 lb. This one 10½ lb. Fractured clavicle due to size. No trouble with cervix.

The indications for the four cesarean sections were as follows: one elective section because of disproportion between pelvic inlet and size of fetal head; two were done because of previous long, hard labors terminated by difficult forceps deliveries. Both of these were sterilized, one had had two previous children and the other, who was 42 years of age, had had one previous child. The fourth patient who had a section was cared for by an out-of-town doctor. She was 38 years of age, had had two children and one abortion, and had her last child sixteen years previous to the section. With this labor she was two to four weeks postmature and she had a large child. After an eight-hour labor, with one-finger dilatation, a section was done and an eight pound, eleven ounce baby was delivered. The patient was sterilized by tubal ligation. The doctor stated, "I do cesarean sections quicker than you would in a large medical center, for

I have more experience with it than I have with a difficult forceps delivery, and this was important in my decision. I was anxious to get a living baby, and a man always tends to use the method he knows best.'' In my opinion, the cervix was not an important factor, if any, in this case.

The patient who had the difficult delivery from below had had four previous long, hard labors with difficult deliveries, due to the fact that the babies were all over ten pounds. With the first baby, the head had to be crushed to effect delivery. The postconization child weighed 10½ pounds and it was delivered by low forceps. Her obstetrician told me that there was no difficulty with the cervix, but because of the size of the child, the delivery was very difficult.

Of the 32 patients who did not carry to term, we had information on 29, and of these, 24 had abortions and 5 had miscarriages in the second trimester of pregnancy.

Of the abortion cases, there were three therapeutic, two induced, and three missed abortions. Five of the abortion cases were endocrine problems, one had had a preconization abortion, six had had at least one postconization full-term delivery. In four, no cause was evident, but all of these cases had well healed cervices.

Of the five who miscarried, two had premature rupture of the membranes, one had lobar pneumonia, one had a serious automobile accident, and the last one had been doing an excessive amount of automobile riding.

Sterility has been mentioned as a possible result of conization. There are many causes of sterility, but we see no reason to think that conization, done with reasonably accurate technique, is one of them. In fact, it seems quite clear that conization puts the cervix in so much better condition in cases of cervicitis that it is a definite aid in overcoming sterility. One of our sterility-problem patients had four full-term deliveries after conization.

Wide conization for cervicitis led to the discovery of early uterine cancer in 16 patients. Eight of the 16 had early carcinoma of the cervix. This emphasizes the importance of removing the affected tissue in a condition for microscopic check of all of it. One of the cervix-cancer patients refused treatment and is dead. The other seven were alive without recurrence: two, 12 years; one, 11 years; one, 8 years; two, 4 years; and one, 2 years, after treatment. These findings emphasize the importance of eliminating this irritated battlefield of epithelia promptly instead of waiting for the first sign of cancer and then trying to catch up with it.

There were eight cases of carcinoma of the endometrium discovered at the time of conization by curettage, which is done *routinely* with conization. All eight were alive and well: two, 10 years; one, 8 years; one, 7 years; two, 4 years; and two, 1 year after treatment. Some men advise against curettage in conjunction with cervical operations, but these cases demonstrate the importance of doing it in every case.

In regard to prevention of cervix cancer by wide conization for chronic cervicitis, no cervix cancer occurred in the 1005 cervicitis cases during the periods of observation, and 407 of them were observed for five to fourteen years.

Summary and Conclusions

Brief historical notes sketch important steps in the efforts, from the early days of gynecology, to create an effective and simple operation for eradicating chronic cervicitis.

My study of the problem resulted in devising a special electrode and technique for making wide conization with the high-tension cutting current. After

devising the electrode and securing its manufacture in 1933, it was subjected to extensive testing, not only by myself but by several other members of the Gynecological Staff of Washington University and Barnes Hospital, and a report of this work with a description of the new electrode was published in 1935, and a further report covering additional cases was made in 1939.

In this 1948 paper there is presented a detailed analysis of a series of 1021 cases of wide conization for cervicitis, 634 of which were followed for two to fourteen years. This analysis of our experiences gives a basis for definite answers to the five questions which prompted the study. These questions will be answered here in the order in which they are given at the beginning of the tabular analysis:

1. Wide conization with suturing heals as well and gives as good ultimate results as the excellent Sturmdorf operation, and without the profuse bleeding and troublesome hemostatic measures which constitute a regular feature of the Sturmdorf procedure.

2. Postoperative bleeding was not troublesome, owing to the hemostatic effect of the high-tension cutting wire. In the eleven cases in which there was some postoperative bleeding, in one it was not from the cervix but from the endometrium and was stopped by curettage. In each of the other ten cases, it was controlled by a single tamponade. The use of routine suturing, as shown in Figs. 7 and 8, has practically eliminated bleeding. In the series, 727 cases were sutured, the unsutured or partially sutured ones dating largely from the earlier and experimental years.

Stricture occurred in only sixteen of the 1005 cervicitis cases during the periods of observation. Most strictures can be handled by office dilatation, only three of the sixteen in our series requiring retreatment in the hospital, as shown in Table II. Concerning routine postoperative dilatation as prophylactic for stricture, we have concluded that it is better to leave the internal os undisturbed except when there is evidence of trouble there. The reasons for this conclusion have already been detailed.

The other additional treatments required for persistent or recurrent cervicitis or for polyp or cyst or other minor condition have already been considered in detail in the analysis and tables.

As to the percentage of cures from the primary conization in the 1005 patients followed for cervicitis, there were 14 who required reoperation (Table III), 67 who required some additional minor treatment to effect a cure, and eight from the questionnaire who still had some undescribed discharge and presumably needed some additional treatment—giving 14 failures and 75 improved. Subtracting the 89 from 1005 gives 916 (91 per cent) cures by the primary conization. Additional cures were obtained by the secondary treatments.

Wide conization for cervicitis combines well with other operations, both vaginal and abdominal. In those cases in which a hysterectomy must be supravaginal instead of complete, conization is particularly helpful in eliminating the menace of continuing cervicitis in the cervical stump.

3. As to the question of conization causing difficulty with subsequent labor, in this series of 1005 conized patients, there were 63 subsequent deliveries at

or near term. Forty-nine of these were first deliveries following the conization, as detailed in Table IV, and in none of them were we able to show evidence of trouble from the conization.

Our experience indicates that there is no substantial reason for denying the benefits of conization to women of childbearing age. In fact, we feel it is strongly advisable that they be relieved of the chronic discomfort of cervicitis and of the cancer menace it carries, and be thus put in better condition for future childbearing.

4. The importance of the outlined conization procedure in the diagnosis of early cancer of the uterus is shown by the fact that in this series wide conization for cervicitis led to the discovery of early carcinoma in 16 patients (8 cervical and 8 endometrial). Endometrial curettage is combined with wide conization routinely, as explained in the description of our technique. One of the cervix-cancer patients refused treatment and is dead. All the other 15 cancer patients were alive and well because the conization and accompanying curettage brought early discovery of the cancer and prompt treatment.

5. Wide conization for cervicitis definitely reduced the incidence of subsequent cervical carcinoma. None of the 1005 cervicitis patients developed cervical cancer during the periods of observation.

The estimated rate of uterine cancer in gynecologic patients generally is 4 per cent.[30] The ratio of cervix to corpus cancer varies much in different series, the average being about 5 to 1, or 80 per cent cervix,[31] which gives a rate of 3.2 per cent for cervix cancer in gynecologic patients in general, and it certainly would be higher in a cervicitis group. Applying the rate of 3.2 per cent to the 1005 cervicitis patients, we find there would have developed 32 cervix cancers in the group. Considering the periods of observation and making generous allowance for possible developments after observation, we feel justified in claiming that the removal of the chronic cervicitis prevented cervix cancer in at least 25 of these women.

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607 North Grand Avenue

Discussion

DR. WALTER T. DANNREUTHER, New York City.—At the time when conization of the cervix with the high tension electric spark was originated by Hyams in 1926, Sturmdorf's tracheloplastic operation enjoyed considerable popularity as a means of removing infected and diseased endocervical glands. The objectives of the two procedures were quite similar, and neither was intended to supplant light cauterization with a fine wire tip for simple ectropion; nor removal of the cervix for an extensively scarred, bulky, and cystic portio. The main purpose of both tracheloplasty and conization was to remove all of the infected endocervical glands with minimum damage to, or sacrifice of, the adjacent tissue, and they were never intended for lesions on the portio. The chief disadvantages of the Sturmdorf operation were the necessity for prolonged hospitalization and anesthesia, and the demonstration by Wolfe of Brooklyn in some 200 cases that, in many, islands of infected glands near the internal os escaped excision by the operation. Using the original electrode designed by Hyams, a high tension cutting current, a fifty per cent cocaine solution for local anesthesia, and correct technique, conization can be done as an office and clinic procedure, and the extent of tissue removal is easily within the control of the operator.

It would be difficult to compile statistics from the huge number of cases in which conization in both private and clinic patients has been done by the members of the gynecological staff at the New York Post-Graduate Hospital alone during the past twenty-two years, but I can say that we have never had occasion to modify the original equipment or technique in the slightest degree. In properly selected cases, subsequent serious bleeding, persistence of leucorrhea, cervical stenosis, and dystocia at the time of labor have never been a problem.

The Hyams electrode conforms to the anatomic fusiform contour and length of the cervical canal, and usually excises the endocervix to the depth of one-eighth of an inch. The high frequency machine must generate a fine, high tension, smooth, cutting current with a minimum of coagulation.

I feel somewhat handicapped in discussing Dr. Crossen's presentation because he is evidently now utilizing the desirable features of conization as part of a procedure which provides for a much wider removal of tissue on the surface of the portio and includes many of the features of a surgical tracheloplasty plus the use of a drain and even radium in some cases, and I have had no experience with it. For mere erosion alone surrounding the external os, or complicating chronic infections of the endocervical canal, we have not found a wide excision in this area necessary, as the subsequent contraction and retraction following the use of the Hyams' electrode have been adequate. What Dr. Crossen has done is to combine the principles of conization and Sturmdorf's sutures in a way which enables him to deal satisfactorily with practically all cases of endocervicitis regardless of the extent of the involvement of tissue. I thoroughly agree with his objection to the use of coagulation, but still feel that the fine wire cautery tip, total removal of the cervix, and hysterectomy have their place in some cases. It seems that Dr. Crossen's composite operation is a competitor with Sturmdorf's tracheloplasty for an extensively pathologic cervix, rather than a substitute for the original conization technique.

Dr. Crossen has presented a commendable and careful analysis of his end results and they speak for themselves.

DR. HARVEY B. MATTHEWS, Brooklyn, N. Y.—As has been stated, there are a multiplicity of methods for the treatment of chronic cervicitis. No one is ideal but some are superior to others largely because the operator using his favorite procedure is more proficient in its execution.

I wish to present the following classification of chronic infections of the cervix, which we believe is of great help in choosing the best method of treatment:

Group 1. The recently lacerated cervix (of three to twelve weeks' duration) with superficial infection; or the nulliparous cervix, the seat of mild gonorrheal or nonspecific infection with or without slight erosion and no cyst formation.

Group 2. The lacerated, eroded cervix of from three to twelve months' duration with somewhat more extensive and deeper infection than in Group 1 and perhaps a few superficial cysts. This may obtain in a moderately deeply infected nulliparous cervix.

Group 3. The lacerated, eroded, everted cervix of two to five or more years' duration, moderately deeply infected and hypertrophied usually with visible cysts. A similar condition is present in the deeply infected nulliparous cervix with or without erosion and cyst formation.

Group 4. The neglected lacerated, everted, eroded, hypertrophied, cystic cervix, deeply and extensively infected and of long duration (fifteen to forty years). Rarely the nulliparous cervix may be similarly deeply and extensively involved.

This classification is simple and gives a thumb nail picture of the extent of the gross pathology present. It, furthermore, affords a convenient way of applying the various methods of treatment for each group. For example, we use the small nasal type of cautery for Groups 1 and 2 and for a few cases in Group 3. Conization is an excellent procedure for Group 2 and many cases in Group 3. Lately we have been using it more frequently than formerly because we feel it has advantages over the cautery for the deeper seated chronic infections. For Group 4 we invariably employ the Sturmdorf operation.

We do not believe, however, that wide conization without suturing is entirely safe. Permanent hemostasis is uncertain and stenosis of some degree is frequent and, in some cases, of such a degree as to require hospitalization for treatment. We have had very little experience with wide conization followed by suturing as described by Dr. Crossen. Certainly his results are excellent—91.4 per cent cured. However, there were 89 cases that required some form of later treatment because of wide conization. Sixteen of these were real strictures of the cervical canal and ten cases had postoperative bleeding that called for treatment. No bleeding case, however, was of a serious nature.

We cannot agree that this procedure requires less time, is easier to perform, and is preferable to the Sturmdorf operation. We still prefer the latter operation because, in our hands, it has all the advantages of conization with suturing and few, if any, of its disadvantages. Under ordinary circumstances it takes no longer to perform; hemostasis is certain; the biopsy specimen is just as adequate for microscopic study; stenosis of the canal should almost never occur (we have had one case in twenty-five years' experience); and the incidence of complications during pregnancy and labor is not appreciably increased.

In conclusion, it cannot be denied that one of the most important claims for conization (any type), but particularly with the wide type, is that it always furnishes an excellent biopsy specimen for microscopic examination. It, furthermore, provides excellent therapy in experienced hands and is frequently superior to cauterization of any type. We do not, however, agree, at least at the present time, that wide conization with suturing is preferable to the Sturmdorf operation which has, in our hands, all the advantages and very few, if any, of the disadvantages of wide conization with suturing.

DR. JOE V. MEIGS, Boston, Mass.—I have always felt that cauterization of the cervix, other than light cauterization of the cervix following delivery, had very little place

in the modern attack upon the diseased cervix. Unquestionably good results will be obtained in some cases. The lasting cure of the diseased cervix and the removal of all of the diseased tissue can only be accomplished by removal of the entire cervix. Amputation, cauterization, and conization at best remove only part of the cervix and although the cervix may heal and look well from the outside, yet diseased tissue may well be buried behind the repair, amputation, or cauterization. If the cervix is truly diseased and needs wide conization it should be more safely handled by total hysterectomy with removal of the entire cervix. The fact that cancer of the cervix was found in eight cases (1.2 per cent) and cancer of the endometrium in eight cases (1.2 per cent) argues that (except for Dr. Crossen's good fortune) conization is not the proper treatment of the diseased cervix and the bleeding uterus.

It is my opinion, in these days of modern surgery, that cross cuts should be eliminated in favor of complete eradication of tissue that is so diseased that radical cauterization is deemed necessary. If patients are to have more children, it is better to do the simplest possible treatment as a palliative and, at a later date, when childbearing is over, a radical procedure removing all diseased tissue.

As I have the opportunity in after years to view cases of mine that had a conization, repair, or cauterization of the cervix, the fact is obvious that these operations simply buried diseased tissue; cystic areas can be seen bulging from behind the healed-over cervical epithelium. This sort of treatment must constitute a menace to patients and, in my own practice, I have had two such patients develop a cancer of the cervix. I believe that in a few patients this treatment can be considered but that for the great majority of patients with diseased cervices total hysterectomy is far safer, more conservative, and much more protective.

I must confess that I do not agree with Dr. Crossen's treatment of the diseased cervix.

DR. JOSEPH L. BAER, Chicago, Ill.—I feel impelled to register a double-barreled comment, one in connection with the interesting compilation presented by Dr. Crossen and one in connection with the comments just read and emanating from Dr. Meigs. I have found cauterization to be completely adequate for all the minor types of visible cervical lesions excepting those which under biopsy proved malignant. This refers to the ordinary erosions, the tremendously hypertrophied erosions, and multiple Nabothian cysts of all sizes. For all of these conditions, I have found the actual cautery to be completely adequate. Our procedure has been, and is, a thorough cauterization in a single sitting, in the office and without anesthesia, the patient being ambulatory thereafter, and being observed for four to six weeks thereafter until the entire cauterized area is thoroughly healed.

The number of hemorrhages, occurring usually at the time of separation of the slough, has been so small as to be completely negligible and completely controllable in the office. There have been no symptom-producing strictures of the cervical canal. The number of strictures of the external os has been exactly two. Each was relieved by office dilatation.

For the very severe, markedly hypertrophied cervices with deep bilateral lacerations, i.e., truly diseased cervices, it is entirely appropriate to do the Sturmdorf operation. In that operation a suture placed bilaterally on the descending branches of the uterine arteries completely controls the bleeding and brings about easy and relatively dry repair of the Sturmdorf type. When there is uterine pathology, it is desirable to remove the cervix with the uterus. We have gone almost entirely from supravaginal hysterectomy to total hysterectomy.

DR. CROSSEN (Closing).—There seems to be some confusion as to the type of case in which wide conization is indicated. We use it in cases of extensive chronic cervicitis with deep-seated cysts, such as the cases described in groups three and four of Dr. Matthews' classification. These are the cases in which we formerly did the Sturmdorf operation. Wide conization is a hospital procedure and it cannot be compared with office cauterization which is used in less extensive cases.

Dr. Meigs' discussion is not only a condemnation of wide conization but applies equally to any cervical operative procedure designed to remove the affected area. Nearly one-half of the patients in our series were in the child-bearing period. They wished to be relieved of the troublesome discharge and the menace of future carcinoma, and yet wished to preserve the

possibility of future childbearing. The other half of the patients in this reported series were past 40 years of age and the involuting uterus and ovaries in such patients do have a certain cancer potential. This latter group can be further subdivided into those in whom the chronic cervicitis was the only lesion demanding treatment, and those who had some additional condition needing treatment, such as a myoma. In this last group, I agree with Dr. Meigs that hysterectomy and bilateral salpingo-oophorectomy is the procedure of choice in patients who are good operative risks. In the group with *no* complicating condition, this extensive abdominal operation seems to me a very drastic treatment for a small but important lesion which, as has been shown, can easily be cured by a comparatively simple procedure which gives excellent results in a very high percentage of the cases. I am sure that had I advised hysterectomy in every case needing wide conization many would have had nothing done.

Dr. Dannreuther mentioned the excellent results obtained by the use of the Hyams electrode. As mentioned in the paper, we found this electrode excellent for use on the less extensive cases and we used it as an office procedure, but for the type of case under discussion it was entirely inadequate.

Dr. Baer states that most cases of cervicitis can be handled by deep cautery. Extensive deep cautery, such as would be needed in extensive, deep cervicitis, has the same disadvantages as coagulation, namely the tissue is not preserved for complete microscopic examination, and healing is delayed by the sloughing tissue. He says that the Sturmdorf operation need not be a bloody one if lateral sutures are placed before the conical excision. We formerly did the Sturmdorf operation and the lateral and circular sutures did help to reduce the amount of bleeding but it was still considerably greater than we get with wide conization. One must *use* any new procedure and get used to it before dropping a reliable method such as the excellent Sturmdorf operation. We have found, as stated in our paper, that wide conization with suture combines the good points of the Sturmdorf operation with the desirable features of the cutting current.

Dr. Matthews' classification of the varying degrees of chronic cervicitis and the treatment applicable to each type is very helpful. Our cases fall under his third and fourth groups. He states that he has found the Sturmdorf operation gives excellent results. He has not tried wide conization and it is my hope that he will give it a trial for his broad knowledge and excellent contributions in this field are well known and his evaluation of results would be helpful to all of us.

(Additional papers presented at this meeting will be included in the February issue.)

Items

American Board of Obstetrics and Gynecology, Inc.

The next written examination and review of case histories (Part I) for all candidates will be held in various cities of the United States and Canada on Friday, Feb. 4, 1949.

Arrangements will be made so far as is possible for candidates to take the Part I examination (written paper and submission of case records) at places convenient for them. Candidates who successfully complete the Part I examination proceed automatically to the Part II examination to be held May 8 to 14 inclusive, 1949, at the Hotel Shoreland, Chicago, Illinois. Notice of the exact time and place of the Part I and Part II examinations will be sent all candidates well in advance of the examination date. Closing date for reapplications for admission to the Part II examination will be April 1, 1949.

New Bulletins are now available for distribution upon application and give details of all changes in Board requirements and regulations made at the annual meeting of the Board held in Washington, D. C., May 16 to May 22, 1948. These relate both to candidates and to hospitals conducting residency services for training.

Application forms and Bulletins are sent upon request made to

American Board of Obstetrics and Gynecology,
1015 Highland Building,
Pittsburgh 6, Pennsylvania.

The following physician is to be included in the list of Diplomates certified by this Board:

Whitely, James Meacham, 508 Medical Arts Building, Portland, Oregon, born 1913, received M.D. from University of Oregon in 1938.

Paul Titus, M.D.,
Secretary.

ROSTER OF AMERICAN OBSTETRICAL AND GYNECOLOGICAL SOCIETIES*

(Appears in January, April, July, October)

American Gynecological Society. (1876) *President,* Ludwig Emge. *Secretary,* Norman Miller, Ann Arbor, Mich. Next meeting, May, 1949, Hot Springs, Va.

American Association of Obstetricians, Gynecologists and Abdominal Surgeons. (1888) *President,* James R. Bloss, Huntington, W. Va. *Secretary,* Leroy A. Calkins, 418 11th Street, Huntington, W. Va. Annual meeting Hot Springs, Va., Sept. 7-9, 1949.

Central Association of Obstetricians and Gynecologists. (1929) *President,* Earl C. Sage, Omaha, Neb. *Secretary-Treasurer,* John I. Brewer, 104 South Michigan Ave., Chicago, Ill. Annual meeting Louisville, Ky., Oct. 23, 24, and 25, 1947.

South Atlantic Association of Obstetricians and Gynecologists. (1938) *President,* S. R. Norris, Jacksonville, Fla. *Secretary,* E. D. Colvin, 1259 Clifton Road, N.E., Atlanta, Ga. Annual meeting at Williamsburg, Va., February 10 to 12, 1949, at the Williamsburg Inn and Lodge.

A. M. A. Section on Obstetrics and Gynecology. *Chairman,* William F. Mengert, Dallas, Texas. *Secretary,* A. B. Hunt, Mayo Clinic, Rochester, Minn. Annual meeting June, 1947.

New York Obstetrical Society. (1863) *President,* Albert H. Aldridge. *Secretary,* Claude E. Heaton, 205 East 69th St., New York 21, N. Y. Second Tuesday, from October to May, Yale Club.

Obstetrical Society of Philadelphia. (1868) *President,* Carl Bachman. *Secretary,* George A. Hahn, 255 S. 17th St., Philadelphia, Pa. First Thursday, from October to May.

Chicago Gynecological Society. (1878) *President,* Herbert E. Schmitz. *Secretary,* Edward M. Dorr, 30 N. Michigan Ave., Chicago 2, Ill. Third Friday, from October to June, Hotel Knickerbocker.

Brooklyn Gynecological Society. (1890) *President,* Henry S. Acken, Jr. *Secretary,* J. Edward Hall, 429 Clinton Avenue, Brooklyn 5, N. Y. First Friday, from October to May, Kings County Medical Society, 1313 Bedford Ave., Brooklyn, N. Y.

Baltimore Obstetrical and Gynecological Society. (1929) *President,* Lawrence Wharton. *Secretary-Treasurer,* John W. Haws, 9 E. Chase St., Baltimore, Md. Meets quarterly at Maryland Chirurgical Faculty Bldg.

Cincinnati Obstetrical Society. (1876) *President,* Stanley T. Garber. *Secretary,* Joseph G. Crotty, 146 West McMillan St., Cincinnati, Ohio. Third Thursday of each month.

Louisville Obstetrical and Gynecological Society. *President,* Rudy F. Vogt. *Secretary-Treasurer,* Glenn W. Bryant, Louisville, Ky. Meetings fourth Monday of each month from September to May, Brown Hotel.

Portland Society of Obstetrics and Gynecology. *President,* Ronald Frazier. *Secretary-Treasurer,* Gifford D. Seitz, 919 Taylor St. Bldg., Portland 5, Ore. Meetings last Wednesday of each month.

Pittsburgh Obstetrical and Gynecological Society. (1934) *President,* James Hodgkiss. *Secretary,* Clarence H. Ingram, Jr., 902 Peoples East End Building, Pittsburgh 6, Pa. First Monday of October, November, December, January, February, March, April, and May.

Obstetrical Society of Boston. (1861) *President,* Paul Gustafson. *Secretary,* H. Bristol Nelson, 1180 Beacon Street, Brookline, Mass. Third Tuesday, October to April, Harvard Club.

New England Obstetrical and Gynecological Society. (1929) *President,* Arthur E. G. Edgelow, Springfield, Mass. *Recorder,* Carmi R. Alden, 270 Commonwealth Ave., Boston 16, Mass. Meetings held in May and December.

Pacific Coast Obstetrical and Gynecological Society. (1931) *President,* Philip H. Arnot. *Secretary-Treasurer,* R. Glenn Craig, 490 Post St., San Francisco, Calif.

Washington Gynecological Society. (1933) *President,* William J. Cusack. *Secretary,* John Parks, 901 23 St., N.W., Washington, D. C. Fourth Saturday, October, November, January, March, May.

New Orleans Obstetrical and Gynecological Society. (1924) *President,* Woodard D. Beacham. *Secretary,* Harry Meyer, 3439 Prytania St., New Orleans, La. Meetings held October, November, January, March, and May.

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*Changes, omissions, and corrections should be addressed to the Editor of the JOURNAL. The number after the Society's name is the year of founding.

St. Louis Gynecological Society. (1924) *President,* A. N. Arneson. Secretary, Paul F. Fletcher, 634 North Grand Ave., St. Louis 3, Mo. Meetings second Thursday, October, December, February, and April.

San Francisco Gynecological Society. (1929) *President,* Albert M. Vollmer. *Secretary,* Daniel G. Morton, University of California Hospital, San Francisco, Calif. Regular meetings held second Friday in month from October to April, University Club, San Francisco, or Claremont Country Club, Oakland, Calif.

Texas Association of Obstetricians and Gynecologists. (1930) *President,* Warren E. Massey. *Secretary,* George F. Adam, 4115 Fannin St., Houston 4, Tex.

Michigan Society of Obstetricians and Gynecologists. (1924) (Formerly the Detroit Obstetrical and Gynecological Society.) *President,* O. W. Picard. *Secretary,* Carl F. Shelton, 910 David Broderick Tower, Detroit 26, Mich. Meetings first Tuesday of each month from October to May (inclusive).

Central New York Association of Obstetricians and Gynecologists. (1938) *President,* Raymond J. Pieri. *Secretary,* Nathan N. Cohen, 713 E. Genesse St., Syracuse, N. Y. Meets second Tuesday of September, November, January, March, and May.

Alabama Association of Obstetricians and Gynecologists. *President,* Gilbert F. Douglas. *Secretary,* Hunter Brown, 1922 South Tenth Ave., Birmingham, Ala.

San Antonio Obstetric Society. *President,* I. T. Cutter. *Secretary,* S. Foster Moore, Jr., San Antonio, Tex. Meetings held first Tuesday of each month at Gunter Hotel.

Seattle Gynecological Society. (1941) *President,* Donald J. Thorp. *Secretary-Treasurer,* Charles D. Kimball, 734 Broadway, Seattle 22, Wash. Meetings held on third Wednesday of each month, Washington Athletic Club.

Denver Gynecological and Obstetrical Society. (1942) *Secretary,* Warren W. Tucker, 1820 Gilpin St., Denver 6, Colo.

Wisconsin Society of Obstetrics and Gynecology. (1940) *President,* Henry A. Sincock. *Secretary-Treasurer,* Edith McCann, 425 East Wisconsin Ave., Milwaukee 2. Meetings held in May and October.

San Diego Gynecological Society. (1937) *President,* P. L. Martin. *Secretary,* Albert P. Kimball, 233 "A" St., San Diego, Calif. Meetings held on the last Friday of each month.

North Dakota Society of Obstetrics and Gynecology. (1938) *President,* Ralph E. Leigh, Grand Forks. *Secretary,* G. Wilson Hunter, 807 Broadway, Fargo, N. D.

Virginia Obstetrical and Gynecological Society. (1936) *President,* Walter McMann. *Secretary-Treasurer,* L. L. Shamburger, State Health Department, Richmond, Va. Next meeting not announced.

Columbus Obstetric and Gynecologic Society. (1944) *President,* Dana Cox. *Secretary,* Zeph J. R. Hollenbeck, 9 Buttles Ave., Columbus, Ohio. Meetings held fourth Wednesday of each month.

Naussau Obstetrical Society. (1944) *President,* Robert S. Millen. *Secretary-Treasurer,* Peter La Mariana, Williston Park, L. I., N. Y. Meetings, bimonthly from October to May.

Bronx Gynecological and Obstetrical Society. (1924) *President,* H. J. Lesnick. *Secretary,* Mark Daniel, 2344 Davidson Ave., Bronx 53, N. Y. Meetings, fourth Monday monthly from October to May.

Washington State Obstetrical Society. (1936) *President,* John H. Fiorino, Everett. *Secretary,* C. Wendell Knudson, Medical and Dental Bldg., Seattle, Wash. Meetings, first Saturday of April and October.

Kansas City Obstetrical and Gynecological Society. (1922) *President,* Joseph G. Webster. *Secretary,* William C. Mixson, 320 W. 47th St., Kansas City, Mo. Meetings, last Thursday, September, November, January, and March; first Thursday, May, University Club.

Los Angeles Obstetrical and Gynecological Society. (1914) *President,* L. G. Baldwin. *Secretary -Treasurer,* Gordon Rosenblum, 6333 Wilshire Blvd., Los Angeles 36, Calif.

North Carolina Obstetrical and Gynecological Society. (1932) *President,* Wallace B. Bradford. *Secretary,* Richard B. Dunn. Meetings semiannually.

The Society of Obstetricians and Gynecologists of Canada. (1944) *President,* William A. Scott. *Secretary,* James Goodwin, 516 Medical Arts Bldg., Toronto, 5. Meetings held annually, date of next meeting to be announced later.

Akron Obstetrical and Gynecological Society. (1946) *President,* S. B. Conger. *Secretary-Treasurer,* Alven M. Weil, 1030 First National Tower, Akron 8, Ohio. Meetings held third Friday of January, April, July, and October, City Club of Akron, Ohio, Bldg.

Minnesota Society of Obstetrics and Gynecology. *President,* Russell J. Moe. *Secretary,* John Haugen, 100 E. Franklin, Minneapolis, Minn. Meetings held spring and fall.

Miami Obstetrical and Gynecological Society. (1946) *President,* Homer L. Pearson. *Secretary,* John D. Milton, 1104 Huntington Bldg., Miami, Fla. Meetings, second Thursday in January, March, May, and November.

Omaha Obstetrical and Gynecological Society. (1947) *President,* Charles F. Moon. *Secretary,* Donald C. Vroman, 813 Medical Arts Bldg., Omaha 2, Neb. Meetings held third Wednesday in January, March, May, September, November.

Oklahoma City Obstetrical and Gynecological Society. (1940) *President,* Gerald Rogers. *Secretary-Treasurer,* Arthur A. Hellbaum, 800 Northeast 13 Street, Oklahoma City 4.

Cleveland Obstetrical and Gynecological Society. (1947) *President,* Robert E. Faulkner. *Secretary,* G. Keith Folger, 10515 Carnegie Ave. Meetings on fourth Tuesday of September, November, January, March, and May at University Club, 3813 Euclid Ave., Cleveland 15, Ohio.

New Jersey Obstetrical and Gynecological Society. (1947) *President,* Herschel Murphy. *Secretary,* Benjamin Daversa, Spring Lake, N. J. Meetings semiannually.

Honolulu Obstetrical and Gynecological Society. (1947) *President,* Frank C. Spencer. *Secretary-Treasurer,* H. McLeod Patterson, 202 King Kalakaua Bldg., Honolulu, Hawaii. Meetings third Monday of each month, Mabel Smyth Building.

Oregon Society of Obstetricians and Gynecologists. *President,* Duncan R. Neilson. *Secretary-Treasurer,* David M. Baker, 520 Mayer Bldg., Portland 5, Ore. Meetings held on third Friday of each month from October to May.

National Federation of Obstetric-Gynecologic Societies. (1945) *President,* Ralph E. Campbell. *Secretary,* Woodard D. Beacham, 429 Hutchinson Memorial Bldg., New Orleans 13, La.

Dayton Obstetrical and Gynecological Society. (1937) *President,* A. D. Cook. *Secretary,* L. O. Frederick, 413 Third National Bldg., Dayton 2, Ohio. Meetings, third Wednesday monthly from September through June at the Van Cleve Hotel.

Dallas-Fort Worth Obstetric and Gynecologic Society. (1948) *President,* Asa A. Newsom. *Secretary,* A. W. Diddle, 2211 Oak Lawn Ave., Dallas 4, Texas. Meetings in spring and fall.

Queens Gynecological Society. (1948) *President,* Moses Cohen. *Secretary,* George Schaefer, 112-25 Queens Blvd., Forest Hills, N. Y. Meetings held third Wednesday in February, April, October, and December, at the Queens County Medical Society Bldg.

Mississippi Association of Obstetricians and Gynecologists. (1947) *President,* Walter Simmons. *Secretary,* Richard H. Street, Jr., The Street Clinic, Vicksburg, Miss. Meetings held semiannually.

Florida Obstetrical and Gynecological Society. *President,* Charles J. Collins. *Secretary,* Dorothy D. Brame, Orlando, Fla. Next annual meeting, Belleair, April 10, 1949.

South Carolina Obstetrical and Gynecological Society. (1946) *President,* Manly E. Hutchinson. *Secretary,* J. Decherd Guess, 200 E. North Street, Greenville, S. C. Meetings held in spring and fall.

Buffalo Obstetrical and Gynecological Society. (1946) *President,* W. Herbert Burwig. *Secretary,* Clyde L. Randall, 925 Delaware Avenue, Buffalo, N. Y. Meetings held on the first Tuesday of October through May at the Saturn Club.

El Paso Gynecological Society. (1948) *President,* F. A. Snidow. *Secretary-Treasurer,* C. C. Stapp, 800 Montana Street, El Paso, Texas.

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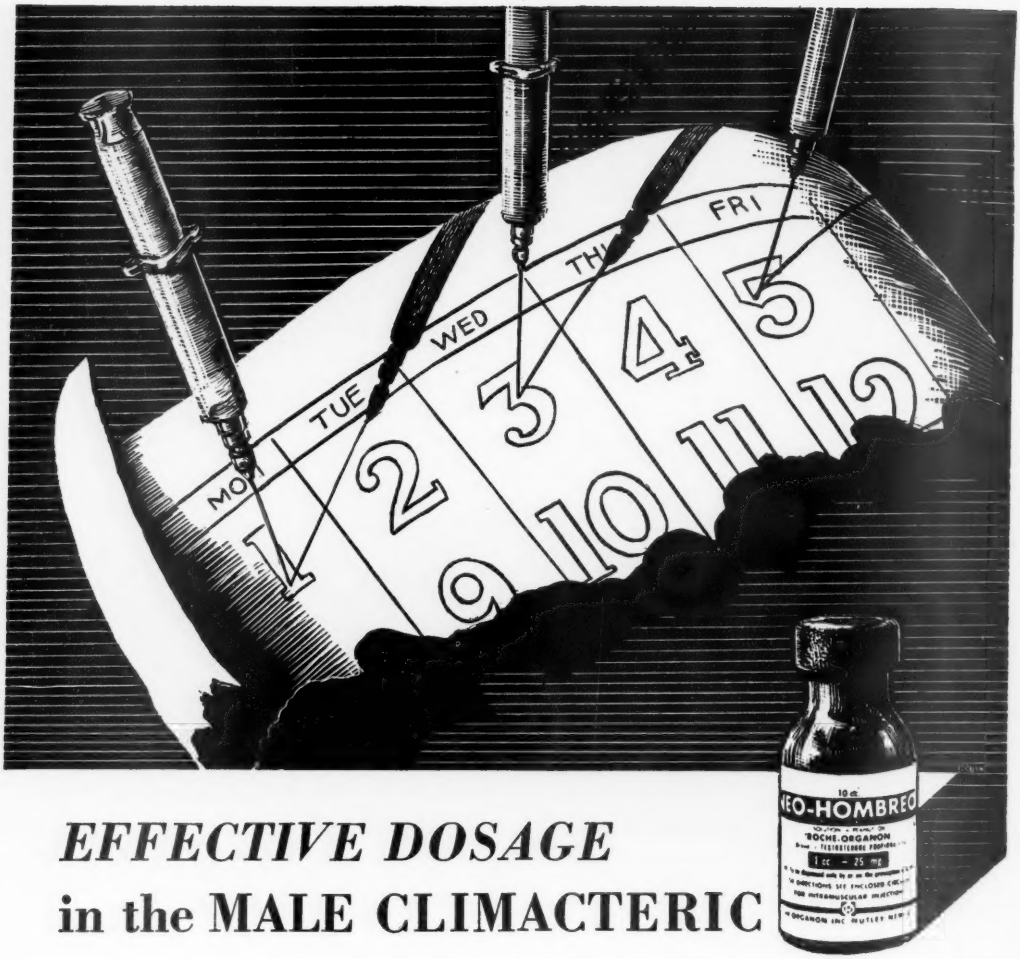

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